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WAR CASUALTIES FROM PROLONGED EXPOSURE TO WET AND COLD

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OUR experiences with casualties resulting from prolonged exposure to wet and cold during the Attu campaign were reported by one of us (RHP) at the October, 1943, meeting in Philadelphia of the Association of Military Surgeons of the United States (5). The cases were classified according to degree of involvement, and general principles of treatment were described. The present paper is submitted in order to amplify several features not previously covered, to discuss problems emphasized by further study, and to report concerning an additional group of cases observed during the past 6 months. Our information has also been supplemented by discussions with medical and other officers who took part in the Attu campaign.

The active phase of this campaign began on May 11, 1943, and ended on May 28, 1943. For periods varying from 3 to 14 days, the soldiers in this operation were exposed to temperatures ranging from slightly above freezing to subzero. Hot food or the opportunity to profit from other artificial or body heat was seldom available. Extremities soon became wet and as a result, natural skin oils were lost. The power of supercooling was thus diminished, and, in the colder areas, this probably allowed some true frostbite.

In all cases the cold penetrated deeply into the tissues, being aided by the diminished circulation from peripheral vasospasm, cramped positions, and general muscular inactivity. The ratio of cooling surface to tissue mass, as well as the moisture acting as a rapid conductor of heat away from the tissues, influenced the distribution and depth of tissue injury. Incidental trauma of walking over rough terrain on the "numb" feet added to the damage.

While exposure continued there was some swelling of the feet with extravasation of fluids into the tissues, small capillary hemorrhages, circulatory stasis, and beginning thrombosis. After several days, when the boots were finally removed, the feet were numb, "like wooden feet," and appeared white or mottled blue and white. Swelling soon increased to a degree that prevented replacement of the boots.

At this time elevation and refrigeration with very gradual warming, as advised by Webster, Woolhouse and Johnston, would have been desirable, but battle conditions and the natural desire of the patient to get warm often prompted wrapping and warming of the limb as quickly as possible. The blood vessels which were first spastic (constricted), now dilated, the extremity becoming warm and the tissues flooded. Extravasation of plasma and

blood into the already edematous tissues increased, as did thrombosis of damaged vessels, circulatory insufficiency, and anoxia and tissue necrosis. On superficial tissues blebs formed, in some cases were broken, and the areas then became infected.

Medical officers and many of the men taking part in the operation commented on the marked variation among different individuals in their susceptibility to wet and cold. Of groups of 3, spending the night in forward listening posts, 2 might return with almost no complaint while the third would have numb, swollen, blue and white mottled feet. This emphasizes the desirability of eliminating beforehand individuals likely to be susceptible to cold, such as those with previous foot or leg injuries, those with signs or symptoms indicating vasomotor instability, those with any suggestion of peripheral vascular disease, and those with foot infections.

It is of interest that one of the battalions spearheading the attack, while suffering battle casualties as high as any battalion in the operation, had only 8 of these foot cases requiring evacuation to the rear. This battalion evidently realized the value of preventive measures, as all of its men had had foot care drills. They had paired off in what they themselves referred to as the "buddy system" where 2 foot-conscious soldiers worked on each others' feet at intervals. Sustained attempts were made to supply the men with an oil or grease to apply to the boots and feet once daily, and provision was made when at all possible to relieve each man (especially outposts) for a few hours daily, during which time he rested in a relatively dry sleeping bag with the shoes and socks removed and drying.

As these men went to Attu direct from established centers in the United States or Alaska and had not previously been subjected to prolonged dietary insufficiency or to dysenteries, etc., they were a group relatively free from extraneous factors which may influence destruction and healing of tissues. They also were free from constitutional diseases such as arteriosclerosis, cardiorenal disease and diabetes, which complicate most cases of gangrene of the extremities seen in civilian practice. The soldiers on Attu had with them, but for the most part threw away, "vitamin C fortified, dried lemon juice," and medical officers state that a few incipient cases of

Fig. 1, left. The only two Japanese prisoners of the Attu campaign received at Letterman General Hospital had gangrenous spots on toes and desquamation on soles of feet.
Fig. 2. One of the two Japanese prisoners had had the right leg amputated. On the left were gangrenous spots; desquamation of skin; and the typical foot deformity seen in these cases, i.e., plantar flexion of great toe and clawing of small toes.

scurvy were noted before the operation ended. There was probably no relationship between this and the local vascular damage of the extremities in these cases, but it might have become an important factor had this campaign lasted much longer.

On admission to Letterman General Hospital, pain, although generally of only moderate severity, was noted in 90 per cent of the cases. Those with gangrene (56 cases) complained of burning pain, most severe at night, in the feet and most often in the toes. They also complained occasionally of aching, pulling, or cramping sensations in the foot or calf muscles. Those without gangrene more often complained of smarting, tingling, and throbbing, mostly of the toes, although often of the balls of the feet. Hypesthesia was present in all cases. In general it began at the ankles and increased to complete anesthesia as the toes were approached. Areas of anesthesia were present in all those with gangrene and about a third of those with desquamation only. The degree of anesthesia was usually, though not necessarily, in proportion to the general severity of the tissue damage. In 2 cases of severe gangrene, necessitating amputation of the entire foot, however, sensation was comparatively unaltered almost to the line of demarcation, while in many showing only a moderate degree of desquamation there was almost complete anesthesia of all the toes. As an indication of the degree of anesthesia, all débridement and all toe amputations were later done without use of any anesthetic and were painless in almost every case.

Correlation of degree of tissue injury with duration of exposure shows that the length of exposure was not the main determining factor in the severity and extent of tissue damage. This again indicated an individual variation in susceptibility to wet and cold. Thus, of the original group of cases received, 76 per cent had only desquamation of the skin and no areas of gangrene; 14 per cent lost toenails, tips of toes, and thick layers of the skin (Figs. 1, 2, 3, 4, 7, and 8); 10 per cent lost one or both feet or portions thereof, such as one or more toes (Figs. 5, 6, 9 and 10). The average duration of exposure for each of the three groups was about the same, 6.5 days. The least severe averaged 6.6 days, the most severe 6.4 days. Three patients requiring amputation of both feet were exposed 4, 6, and 8 days, respectively.

MECHANICAL RESPIRATION AND OXYGEN THERAPY

Twenty-one patients were treated by mechanical respiration, produced by alternating positive and negative pressure on the thorax. The mechanical device used was the Terhaar

Fig. 3, left. Apparent deep gangrene which later was found not to extend as deep as was first believed. (See Fig. 4.)

Fig. 4. Same feet as in Figure 3, 1 month later. Toes present, only part of nails being lost.

Fig. 5, left. Gangrene of toes, which eventually came to amputation. Compare with Figures 3 and 4, where tissue damage of two toes of left foot was more apparent than real.

Fig. 6. Same feet as in Figure 5, 8 weeks later. Gangrene resulting in loss of toes.

respirator, made in two half shells which, when clasped together, encircle the chest. The rationale for this treatment is as follows:

By increasing the negative pressure in the thorax, there may be induced a change in pressure gradient between that part of the venous and lymphatic bed which lies inside the thorax and that part of the venous and lymphatic tree which is distributed outside the thorax. If true, this should result in an increased

Fig. 7, left. Extreme degree of desquamation. Marked cavus and claw foot tendency seen in many of these cases.

Fig. 8. Same feet as in Figure 7, about 4 weeks later. Cavus present. Heavy skin all off. Ulcer left great toe almost healed. Feet tender, balls of feet and toes still anesthetic, 8 weeks after exposure.

Fig. 9. Feet and knees 3 weeks after exposure. Knee ulcers due to crawling, after feet were numb. Feet bluish black; boggy, moist, infected zone at line of demarcation. Gas infection developed 5 weeks after exposure. (See Fig. 10.)

venous and lymphatic return to the heart, a more efficient cardiac output, and in cases such as these an improved capillary flow by the removal of venous stasis and edema.

Mechanical respiration probably differs from the pavex boot in the following physiological principles: The boot exercises its negative pressure entirely on the peripheral circulation, and may thus increase capillary trauma and extravasation; the chest respirator seems to produce its effect by improving the deep venous and lymphatic return to the heart, thus

Fig. 11. Same patient as in Figures 9 and 10. Amputated specimens have been sectioned in the sagittal plane. Deep tissue necrosis present.

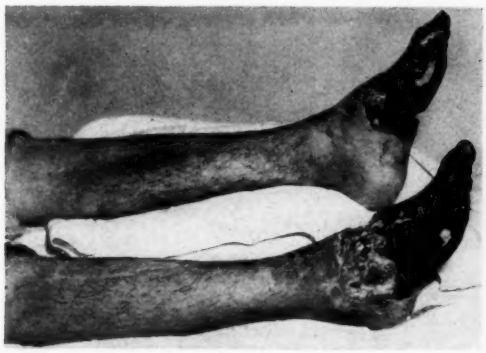

Fig. 10. Same legs as in Figure 9. Foot became mummified, but wide soft moist line of demarcation remained. (See Fig. 11.)

improving capillary flow by producing a more favorable gradient between the arterioles and venules.

The pressure differentials used were a negative pressure of 10 millimeters of mercury, alternating with a positive pressure of 4 millimeters of mercury. This was given at the rate of 18 respirations per minute. Oxygen was administered at the rate of 3.5 liters per minute in a further effort to relieve local tissue anoxia. One hour treatments were given once daily or twice in severe cases.

It was not possible to group the cases in which patients were treated by the respirator and oxygen with comparable control cases with sufficient accuracy to draw a definite conclusion as to end-results. There seemed to be, however, a favorable effect on the lower extremities demonstrated by improvement of color of affected portions and reduction of congestion and edema.

Fig. 12. Same patient as in Figures 9, 10, and 11. Amputations have been performed 2 weeks before, just above ankles, stumps left open, stockinette secured by glue and cut into four strips for traction over pulleys at end of bed. Revision of stumps to be done later if necessary.

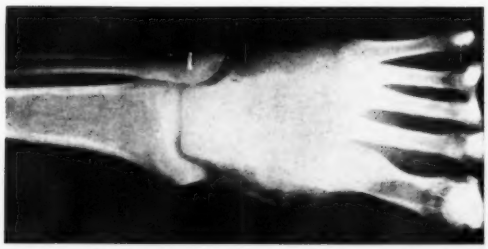

Fig. 13. Gas pockets in soft tissues between metatarsals and medial and lateral aspects of the foot.

Despite the favorable local changes here noted, it is our opinion that the optimum time for beneficial use of such measures is during the hours and days immediately following the initial trauma. Then the improved venous drainage plus the better tissue oxygenation might be expected to result in an appreciably lessened tissue necrosis.

Although the advisability of some artificial means of improving lymphatic and venous drainage without at the same time increasing local exudation has been previously mentioned (7), it is believed that this represents the first practical application in such cases.

The mechanical respirator and oxygen therapy treatment used on the group of patients discussed was carried out by Captain Robert A. Kennedy, M.C.

GAS INFECTION AND X-RAY FINDINGS

In patients with gangrene, cultures taken from the moist demarcating areas at the first dressing at Letterman General Hospital showed a profusion of mixed organisms, including streptococci, staphylococci, pseudomonas pyocyaneus, and members of the colon group. However, infection remained localized to the demarcating zone in all except 1 case.

The patient in this case, with gangrene of one foot, complicated by a gunshot wound just above the knee, developed a spreading moist gangrene of the lower leg, accompanied by markedly elevated temperature and pulse. At amputation just below the knee gas pockets and exudate, typical in appearance and odor to that of gas gangrene, were found throughout the tissue planes. Anaerobic cultures of the exudate and tissues were negative, while aerobic cultures revealed only Staphylococcus aureus, nonhemolytic streptococci, Streptococcus viridans, and paracolon bacillus.

Fig. 14. Roentgenogram showing calcium undisturbed in proximal phalanx of gangrenous foot because there was no blood supply, whereas marked loss of calcium was present in corresponding bone of opposite foot where blood supply was good.

In 2 patients with extensive gangrene of both feet, cultures revealed the presence of Clostridium welchii. In neither case were there toxic symptoms, and after amputation there was no further evidence of the infection. Dissection of these feet showed both liquefaction and gas formation with positive cultures in superficial and deep tissues. As this occurred 35 days after exposure, it represented a fairly well localized gas bacillus cellulitis, rather than the classical rapidly spreading and highly toxic myositis.

Three other patients with extensive gangrene, in whom anaerobic cultures were consistently negative, showed by x-ray multiple circumscribed rarefied areas in the soft tissues of the feet (Fig. 13).

The significance of such x-ray findings is at times doubtful as separation and retraction of dry gangrenous tissues, as well as liquefaction of tissue, will alone or in conjunction with gas-forming organisms, produce similar changes in tissue density. Such changes may also be produced by other organisms such as anaerobic streptococci, along with various aerobes, as Streptococcus pyogenes and Staphylococcus

Fig. 15. Zone of demarcation in one of amputated feet (Fig. 11). Granulation tissue heaped up over epithelial margin and deep inflammatory infiltration; amputation 6 weeks after exposure. ×70; hematoxylin eosin stain.

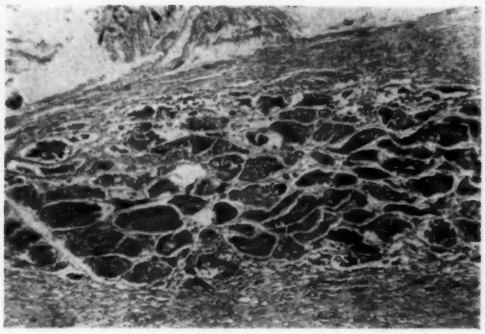

Fig. 16. Skeletal muscle from one of the amputated feet, above zone of demarcation, showing atrophy, degeneration, and a chronic inflammatory reaction. Photomicrograph ×80; hematoxylin and eosin stain.

pyogenes (4). One differential point is that changes in tissue density which are due to retraction or liquefaction generally manifest themselves slowly and may vary little from week to week, while changes due to gas gangrene may come on more suddenly and spread more rapidly, the more severe cases being accompanied by symptoms and signs of toxicity.

All patients in whom gas bacillus infection was suspected, in addition to sulfa drugs or penicillin or both, were given prophylactic x-ray treatment of 50 to 100 r twice daily for 3 to 5 days, as advised by Kelly and Dowell.

The x-ray also revealed in most cases a decalcification of nearly all the bones of the feet, probably due to immobilization. Where complete deep necrosis had taken place and there was loss of blood supply to the tissues, the bones were white and dense, little or no calcium being lost (Fig. 14).

VENOUS SYSTEM COMPLICATIONS

One patient who came to midmetatarsal guillotine amputation because of gangrene and cellulitis of the distal half of the right foot developed phlebitis of the greater saphenous vein. He was treated with dicumarol and two lumbar sympathetic intracaine blocks, and rapid subsidence of the phlebitis resulted.

Another patient, seen 7 months after exposure, had had a phlebothrombosis of the left superficial femoral vein following left inguinal herniorrhaphy in 1937. Resulting varicose veins were treated by ligation and division of the lesser saphenous trunk in February, 1942. Following the exposure on Attu, deep phlebothrombosis flared up and was treated by rest and bandages. Eight months after exposure there was still moderate aching and swelling of the leg on more than minimal standing or walking. Venograms revealed irregularity of the posterior tibial vein, no visualization of the superficial femoral vein, and development of a narrow, tortuous anastomotic channel lying just medial to the femur. Incompetent perforating veins carried the blood from the posterior tibial to the greater saphenous vein just below the knee, this serving as the main channel of venous return in the thigh. This soldier might well have been eliminated from the group prior to invasion of the islands. These were the only two venous system complications of this type occurring in the group.

Following second degree involvement, 2 cases went on to the Southwest Pacific. Slight symptoms increased, and 10 and 11 months, respectively, after exposure these 2 patients were returned to the mainland. There was aching pain and cyanosis to just above the ankle on one lower extremity. There was no edema. The dorsalis pedis and posterior tibial pulses were weaker than on the opposite side. Venograms of both lower extremities were normal. This unilateral cyanosis of one foot was more pronounced when the extremity was dependent. The condition probably was due

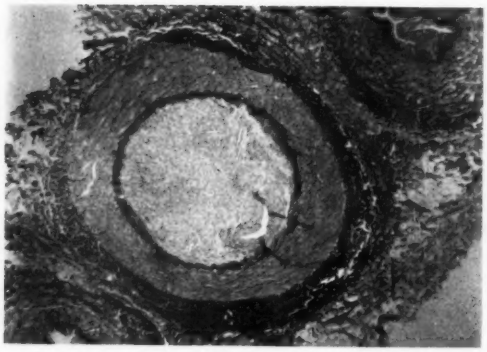

Fig. 17. Posterior tibial artery and veins of amputated foot, showing thickened media, and organized, recanalized thrombus; 4 cm. above zone of demarcation. Photomicrograph ×70; hematoxylin and eosin stain.

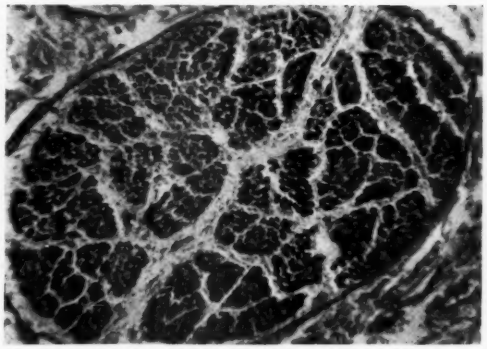

Fig. 18. Microscopic section of nerve of the same foot, 7 centimeters above the zone of demarcation; the myelin sheaths are intact. Photomicrograph ×225, Weigert stain.

to local changes in the foot brought on by the exposure.

TISSUE DAMAGE AND AMPUTATIONS

Difficulty in distinguishing the severity of the injury, identifying viable from nonviable tissue, whether due to heat or cold, has always been notable and was experienced with these cases. By delay, moist gangrene will sometimes extend, but more often, what is apparently extensive gangrene may be less extensive than is at first suspected. A black superficial tissue shell may peel off to disclose toes still covered with epithelium (Figs. 3, 4, 7 and 8).

Before amputating, most surgeons wait until there is a complete mummification of dead tissues with retraction or separation of the nonviable portions at the line of demarcation. However, no patient seen by us progressed to complete mummification, all patients retaining a broad, moist infected area at the demarcating zone (Figs. 5, 9 and 10).

Amputations of toes or parts of feet, for the most part, were done on our cases 5 to 9 weeks after exposure, and in some cases might well have been done earlier. Such amputations should be done as soon as it is determined that there is no chance of saving the part. Dead tissue left in place harbors organisms, aids in the spread of infection to normal tissues, increases fibrosis and consequent formation of deep scar. Removal of dead tissue is comparable with the early removal of deeply necrosed tissue from a burned area, now advised by many as a primary treatment in burns. Any method that will differentiate between viable and nonviable tissues should be used. Dingwall, using sodium fluorescein, has been able, with a fair degree of accuracy, to determine a second from a third degree burn. It would be a great step forward if this method should prove of value in cases of varying degrees of gangrene of the extremities.

Amputations of toes should be done just distal to the apparent zone of demarcation. The bones should be cut across as gently as is possible, preferably with a small saw, and then trimmed with a rongeur to a level a few millimeters above that at which the soft tissues are cut. Care in sectioning the bone will prevent fractures that might aid in the spread of infection. In cases with most marked infection trimming of the bone ends may be left until a week after the soft tissue amputation by which time the infection will have subsided and the danger of osteomyelitis be lessened. A similar open procedure through the midportion of the foot may be performed if it is thought that a satisfactory stump can be obtained.

In cases in which the foot has been damaged severely enough to preclude the probability of success with one of the proved classical foot amputations, a sleeve guillotine amputation should be done above the ankle

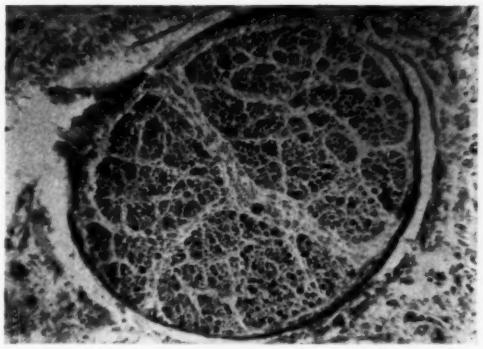

Fig. 19. Section of the same nerve as shown in Figure 18, 3 centimeters above the zone of demarcation, showing pronounced loss of myelin. Photomicrograph, ×225, Weigert stain.

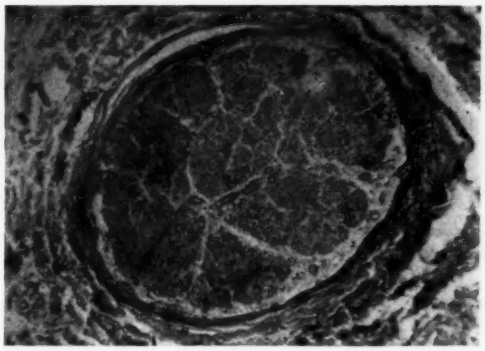

Fig. 20. Same nerve 1 centimeter above zone of demarcation showing almost complete loss of myelin and proliferation of perineurium, epineurium, and endoneurium. Photomicrograph ×225, Weigert stain.

and well above the questionable zone. Later on, a plastic revision or reamputation may be done. Compression bandage and traction on the stump by skin glue and stockinette should be used following the guillotine operation (3). Such stumps usually heal very rapidly (Fig. 12).

Vaseline gauze packs and infrequently changed occlusive dressings over infected or granulating areas are to be condemned, for, as with the gangrenous parts themselves, when left in place drainage is blocked and there is a tendency for the infection to pool or spread.

All granulating areas, even the small ones, should be prepared for early skin grafting. Normal saline dressings, changed two or three times a day, have been the most satisfactory means of preparing the granulating area for grafting. Dakin's solution, moist penicillin dressings, and other preparations have been used in selected cases but have failed to demonstrate any appreciable superiority to saline.

PATHOLOGICAL FINDINGS

Careful dissections were accomplished on the amputated extremities and sections of the larger nerves and blood vessels were taken for microscopic examination from various levels at and above the zone of demarcation.

Below the zone of demarcation the tissues were necrotic and infiltrated with polymorphonuclear leucocytes. At the ulcerated demarcating zone granulation tissue penetrated quite deeply below the surface (Fig. 15) Above there was a moderate edema and a subsiding, spotty, organizing, inflammatory reaction penetrating along the fascial planes. A loose connective tissue infiltrated with inflammatory cells replaced much of the usual fatty tissue. Muscles showed considerable areas of destruction and replacement with fibrous tissue, degenerated muscle bundles being in places scattered throughout a loose fibrous stroma as isolated groups of fibers (Fig. 16).

Examination of arteries and veins at the various levels indicated that some had undergone thrombosis and recanalization: others revealed marked acute endothelial proliferation with edema of the walls and focal fibrous thickenings; in some there was practically no change (Fig. 17). The vessels were usually thrombosed near the site of demarcation, while distal to that level they were necrotic and almost indistinguishable from the other tissues. Thrombosis, even where canalized, did not extend more than 3 to 5 centimeters proximal to the demarcating zone. Arteries and veins seemed equally affected.

The nerves at the level of the amputation, about 10 centimeters above the zone of demarcation, showed the myelin sheaths apparently intact. As the demarcation zone was approached more and more sheaths in each nerve revealed either complete or partial loss with distortion of the myelin. At the

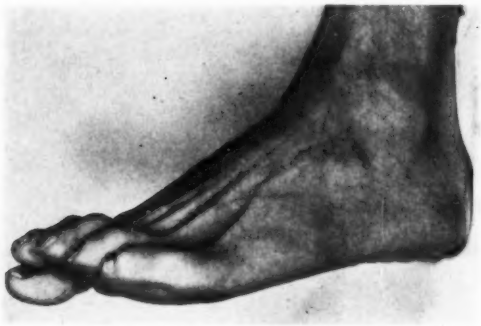

Fig. 21. Eight months after exposure. This deformity was present to some degree in most cases. The great toe pulls downward, small toes upward, and cavus of foot is increased.

actual demarcation zone, myelin had completely disappeared, as verified by special staining processes. The highest level of demyelinization was quite irregular in the various nerves examined (Fig. 18, 19, and 20).

It must be remembered that these pathological changes were noted in specimens obtained by amputation, averaging about 6 weeks following the initial trauma. No tissues showing pathological changes soon after exposure were available. However, the findings in our specimens were those that might be expected to result from the earlier tissue edema, necrosis, and arterial and venous thrombosis, described elsewhere.

FOOT DEFORMITIES

A majority of patients seen, even including those with only second degree damage, developed a foot deformity. This was generally of a claw foot type, with varying degree of pes cavus. The great toe was pulled downward into plantar deformity and the intervals between all of the toes were increased (Fig. 21).

The mechanism of production of this rather characteristic foot deformity is probably as follows: The muscles of the foot consist of two groups—the long extrinsic ones from the leg and the short intrinsic ones within the foot. There are flexors and extensors in both groups. An intricate balance of all these muscles is necessary for the proper functioning of the foot. It is generally recognized that on prolonged disuse, muscle atrophy is more marked in the intrinsic group than in the extrinsic group. At the time of original exposure, chilling and anoxia of all tissues of the feet were probably greater than of the deeper tissues of the leg. This resulted in greater damage to the intrinsic muscles of the feet and their nerve and blood supply, than to corresponding structures higher in the leg. Thus the muscles of the foot were first weakened by direct damage and secondarily by atrophy of disuse with a resultant imbalance in favor of the long muscles. The long extensors to the 2nd, 3rd, 4th and 5th toes then pulled the metatarsophalangeal joints into dorsiflexion while the long flexors, uninhibited by the atrophied antagonistic intrinsic muscles, pulled the interphalangeal joints into marked plantar flexion. The flexors to the great toe being stronger than the extensors resulted in a plantar contraction of that toe (Fig. 2, 4, 7, and 8). The increased interval between the toes was due to the swelling of the tissues, plus the fixation in contraction of the lumbrical and interosseous groups. Some degree of pes cavus is produced by the contracture of the muscular and fascial structures in the plantar aspect of the foot. The appearance of cavus is exaggerated, however, by atrophy of the plantar soft tissues and by the plantar deformity of the great toe. This deformity reached its height at around 4 to 6 weeks, and then tended to subside partially with lessening of the swelling. A permanent destruction of many muscle fibers no doubt occurs in some of these cases, and this, together with replacement fibrosis and scarring in the swollen and damaged muscles and fascial planes (see "Pathological Findings"), tends to produce permanent weakness and contractures. The importance of the deformities thus produced as primary factors in later disability cannot be overemphasized as they may be very persistent, even in second and third degree cases. Of 11 third degree cases (not severe enough to lose toes) observed here 8 to 10 months after the original exposure, 6 had pes cavus and claw toe deformity that evidently contributed materially to deep foot pain on walking. A persistence of marked limitation of dorsiflexion of the great toe due to contracture of the toe flexors was present in 2 of these.

These findings call attention to the importance of proper support during the acute phase following injury of the extremities and to early and continued active exercises to prevent or lessen permanent deformity. Exercises should be continued after the patient is ambulatory and arch supports or other types of shoe corrections will be found desirable in many instances. In the late cases (8 or more months after injury) observed by us, such foot deformities limited exercise and walking almost as much as the more generally recognized superficial burning pains of the feet. The delay in nerve regeneration in such cases was illustrated by findings of hypesthesia to complete anesthesia of the skin of the toes in all cases. On 2 the hypesthesia extended 3.5 centimeters above the toe webs.

CONCLUSIONS

1. Individuals likely to be susceptible should avoid prolonged exposure to cold and wet, and in the case of soldiers, the susceptible ones should be eliminated before being moved into such areas.

2. A type of mechanical respirator which seems to improve venous and lymphatic return from the extremities may prove of value, especially in the early treatment in such cases.

3. In treating patients with gangrene of the extremities, routine, periodic, x-ray films and wound cultures (aerobic and anaerobic) are advised.

4. Tissue retraction and liquefaction in gangrenous soft tissues may produce radiological changes hard to differentiate from those due to gas-forming organisms.

5. These cases do not proceed to the classical mummified dry gangrene types. Amputation should be performed as soon as viable and nonviable tissues can be differentiated.

6. Pathological studies revealed diffuse spotty fibrosis, thrombosis and recanalization of blood vessels, total demyelinization of nerves at demarcating zone regressing to normal appearance 10 centimeters above this zone.

7. Characteristic foot deformities and the mechanism of their production are described.

8. Eleven cases, 8 to 10 months after injury, have been observed.

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SIMPLIFIED DESIGN FOR REPAIR OF SINGLE CLEFT LIPS

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SIMPLIFICATION of the design for incisions in repairs of cleft lips may allow more time for concentration on the fundamentals involved in shifting the tissues into position and their fixation, and better results may be obtained.

TYPES OF OPERATIONS

V-excision of the cleft and bringing the edges together is the most simple type of repair for single cleft lips (Fig. 1). This plan has been used by many surgeons, with good results, particularly in partial clefts. One objection to it is the straight-line scar which may contract to produce a notch or "whistling deformity." Another objection is that the lip which is produced comes straight down (as seen in the profile view) from the nostril floor to the vermilion.

The normal lip curves forward (in profile) just above the vermilion border. This "break" normally occurs about two-thirds or three-fourths of the way down the lip and a repair which reproduces this "kick-out" of the vermilion and the skin just above it will more closely resemble a normal lip (Figs. 11 to 18). To do this, one needs to use a design which will give an extra amount of tissue in this region, and to close the tissues firmly up toward the top of the fornix on the inside.

The Mirault operation, a description of which was published over one hundred years ago, takes this into account and provides extra tissue at the border by means of a small triangular flap. Mirault used flaps from both the columellar and alar sides of the cleft, but his and subsequent experience has shown those from the alar side to be better. This was noted in 1929 by Blair and Brown (1), but the standard flap which was described then was half the length of the lip and this has been found to be too large in some patients.

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The main principle of the operation remains just as desirable as ever, but better results may be obtained by using a small flap to produce the fullness in only the lower one-third or one-fourth of the lip. The simplified plan of marking, outlined below (Fig. 1), has been used for 7 years. It has facilitated the entire operation, has made the teaching of it easier, and has caused some interest to be developed by house surgeons who often appeared bored before.

The essentials of the plan are that (1) A V-excision operation is marked out first; (2) then instead of completing this operation, a small flap is designed on the cleft side to turn down and across to the central side. This saves tissue, fills out the lower border, and (when careful mucosal closure is done) leaves a protruding lip.

At the primary operation, it is of major importance to obtain: (1) a symmetrical alar level; (2) a good alar direction toward the columella; (3) satisfactory nostril floor; (4) a normal nostril curve, that is—across the tip; (5) a straight columella; (6) a full lip border in advance of the lower lip with a normal concavity from above downward (this might be called a flexion crease); (7) a full vermilion without a notched "whistling deformity." It is necessary to get primary healing, but this is usually not difficult if care is taken in the accurate apposition of raw surfaces and in avoiding tension by the wide mobilization of surrounding facial tissues.

Anesthesia. Ether vapor seems to be the safest sedative for babies. If both infraorbital nerves are blocked by injecting 2 per cent novocain around the region of the foramina, much less ether will be needed. The vapor is blown through a long, curved, sterile metal tube which is held about 1 or 2 inches from the mouth. The anesthetists are encouraged to give just enough so that the baby will remain reasonably still, but not enough to

Fig. 1.

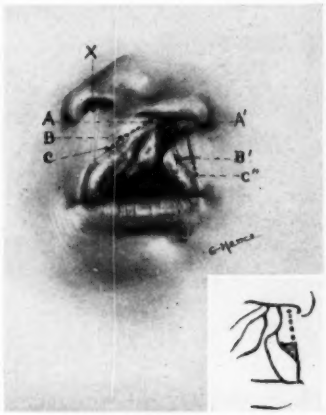

Fig. 2.

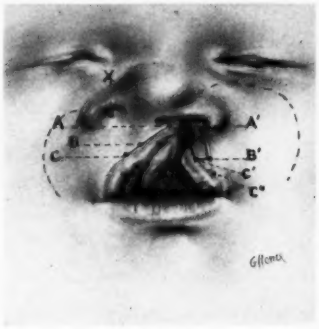

Fig. 3.

Fig. 1. The V-excision operation. While the columella is held over straight, A is marked at the junction of the skin and vermilion at the level of the base of the columella. X is in the same relation to the columella on the sound side. A' bears the same relation to the ala on the cleft side that X bears to the ala on the normal side. C is on the mucocutaneous junction at the point where the vermilion first begins to thin out. C'' is on the mucocutaneous junction, the same distance from A' that C is from A. To do the V-excision operation, A' is brought over to A and C'' to C, after excision of the edges of the cleft.

Fig. 2. The flap operation. The V-excision operation is marked out first. C' is on the mucocutaneous junction at the most medial point of good full vermilion. B' is on the line A'–C'', equidistant from C' and C''. The incision is A'–B'–C' saving the amount of lip indicated by the shaded isosceles triangle in the insert drawing. B is on the mucocutaneous junction, the same distance from C that B' is from C'.

Fig. 3. The lines A–B–C and A'–B'–C' are lightly incised with a knife. The incision is carried upward from C' on the mucocutaneous junction to separate the vermilion from the skin. This is also done at A to keep any vermilion out of the nostril floor. The circular dotted lines show the area which is to be undermined at the next step.

abolish the cough reflex, and it is better to err on the light side. An assistant uses a sucker from time to time to keep the mouth clear of blood. The operator sits above the head of the patient, thus seeing the face upside-down throughout the operation. Intratracheal gas-ether is used when the patients are old enough (in adults, local anesthesia usually suffices).

The marking is done with care after due consideration of all of the elements of deformity in the individual patient. Time spent at this stage will save operative time later because a good design can be followed throughout the operation without change. A mechanical drawing pen and 5 per cent alcoholic methylene blue are used, puncturing in the dots, scratching in the lines, and wiping off any excess dye with an alcohol sponge.

MARKING OUT THE V-EXCISION OPERATION

To mark point A, the columellar side of the lip is pushed over into the cleft until the columella is straight and in the midline. A is then punctured near the mucocutaneous junction on the level of the base of the columella. (It may be put in on this line while it is still in its diagonal position.) Point X is punctured in the floor of the other nostril in a position corresponding to A (Fig. 1).

The relationship of X to the curve around the base of the normal ala is noted. A' is then placed in the same relation to the base of the ala on the cleft side. If it is difficult to determine the grooves between the ala and cheek and lip, these landmarks can usually be brought out by temporarily pushing the lip medially over into the cleft.

C is on the mucocutaneous line, at the medial end of the full thickness of vermilion. This point, where the vermilion first begins to thin out, can be best ascertained by looking at the lip from above. At times it is almost over to the philtrum on the normal side.

C'' is on the mucocutaneous line, the same distance from A' that C is from A. A small caliper is useful for measuring these distances.

Fig. 4. Incisions made in the buccal fornix on both sides and the soft tissues of the lip and cheek are taken loose from the bone, up almost to the lower border of the orbit on the cleft side. Less extensive mobilization may be necessary on the sound side, though it is sometimes necessary to elevate that nostril up out of the pyriform recess and to cut the base of the septum slightly before the normal ala and columella can be straightened. In any event, the mobilization is continued until the nose can be straightened and the two sides of the lip can be brought together without tension.

Fig. 5. Undermining between the lining and skin of the nostril so that they will slide on each other when the nostril is rolled up into a tube. At times it is necessary to make the little vertical cut shown just in front of the turbinate to allow complete rotation of the nostril.

(To do the V-excision operation, lines are drawn from A to C and A' to C'', the edges of the cleft are excised accordingly and fitted together.) This operation is not used except in a few partial clefts and in a few secondary operations. It is the easiest design to carry out.

MARKING OUT THE FLAP OPERATION

The V-excision operation is marked out first. C' is then located on the mucocutaneous junction at the highest point where the vermilion on the alar side is still of full thickness. This point, where the vermilion first begins to thin out, is again most easily seen from above the patient (Fig. 2).

B' is on the line A'–C'' and equidistant from C' and C''. The isosceles triangle C''–B'–C' is the Mirault flap and is the additional amount of lip which is saved by this operation. B' is usually about one-third or one-fourth of the way up from C''.

B is on the mucocutaneous line and the same distance from C that B' is from C'.

Discussion of marking. Any error in placing A' should be on the low side. The lower the mark, the higher the cleft nostril will be and this is the reverse of the common deformity.

An additional check can be had by measuring the distance from X vertically down to the mucocutaneous junction. A–C should not be greater than this distance, or the lip will be too long, a common error.

Both C and C' should be opposite good thick vermilion. This is one of the instances in which two halves cannot be satisfactorily joined to make a whole, and if either of these points is opposite thin vermilion, a "whistling" defect is almost certain to result. However, if either of the points is placed too far laterally, an unnecessary amount of lip will be sacrificed.

Due to the curvature of the surface of the lip, one is measuring "air distances" rather than "ground distances" in locating all of these points. This would seem to be a source of error, but in practice these inequalities usually cancel each other.

THE OPERATION

After one is satisfied with the marking, the lines A–B–C and A'–B'–C' are lightly incised with a knife. The mucosa is also divided from the skin above A up in the nostril. The incision on the other side from C' is carried upward into the nostril along the mucocutaneous junction. A rectangular skin flap is thus outlined between C' and A' and may be used

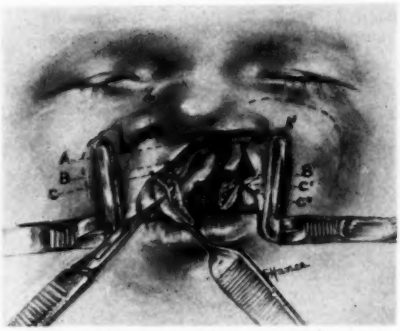

Fig. 6. The lightly incised lines A–B–C and A'–B'–C' are cut completely through the lip with a stab blade, with care to keep knife exactly perpendicular to lip. All angles should be completely opened. The vermilion is inspected and any attached skin removed with a stab blade. The rectangular flap freed from A'–B'–C' must be loose enough to be rotated up 180 degrees into nostril floor. Dotted lines indicate area undermined.

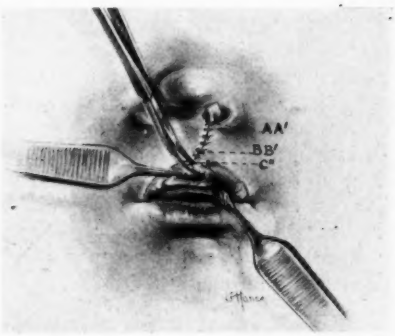

Fig. 7. A and A' are approximated with a deep stitch of white silk or cotton or No. 000 catgut (knot on the mucosal side) and a surface suture of No. 000 black silk. B and B' are approximated with a fine deep white stitch and a black one on the surface. Intervening fine surface sutures are placed and an oblique cut is made in the vermilion flap from C'. For the incisions and trimming fine, very sharp scissors are most useful.

later, if necessary, to form the nostril floor by rotating it 180 degrees up into place (Fig. 3).

Mobilizing the lip and nose. An incision is made in the buccal fornix on the cleft side, extending from the molar region forward to the cleft (Fig. 4). The soft tissues of the cheek are elevated carefully from the bone up toward the orbital border. This freeing of the cheek should allow that side of the lip to be brought easily across the cleft and the nostril to be rotated into its proper position. If tightness of the lining of the nose prevents this, it may be necessary to make a small vertical incision in front of the anterior end of the inferior turbinate (Fig. 5). After the lip and ala are freely mobilized, small scissors are

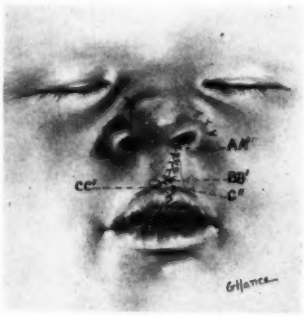

Fig. 8.

Fig. 9.

Fig. 10.

Fig. 8. C and C' are united and the vermilion flaps are interdigitated in a zigzag fashion, fitting them so that they lie naturally together without any pull or stretching. Suturing is then continued on around the vermilion border and up the inside to the fornix. The little flap in the nostril is trimmed to fit with the one from the opposite side, and they are sutured together to form the floor. A few key mattress sutures are placed through the ala to unite the lining and covering (which were separated during the undermining).

Fig. 9. The mucosal suturing is important and is done with fine interrupted stitches and careful trimming to fit the edges together. The upper corners are rounded somewhat, and the suturing is continued to pull some mucosa into the lip from either cheek. This advances the whole lip and thrusts it forward. If the superior edge of the mucosa is tight, vertical slits are made on either side and allowed to spread open.

Fig. 10. Normal profile of an infant showing the upper lip far in advance of the lower and the flexion crease in the upper lip with the forward thrust of its lower border. This gross contour of the upper lip and its relations to other features is visible and noticeable at a greater distance than are some of the finer details of the lip.

introduced through the buccal fornix and the skin of the nose is elevated throughout the lower half and over across the midline toward the normal side (Fig. 5). This tends to minimize "corrugation" of the lining when the nostril is rotated inward and up to its new position, and possibly helps establish a columellar-alar angle instead of the straight line that is present here in wide clefts. The undermined cheek is packed temporarily with one-fourth strength adrenalin on gauze.

Similar mobilization of the lip (but not the nose) is done on the opposite side, though it is usually not so extensive. If the nose is badly deviated, it may be necessary to elevate the base of the normal ala up out of the pyriform recess with a small periosteal elevator. Sometimes it may also be necessary to make a small cut across the base of the septum underneath the lip. When mobilization is complete, the two sides of the lip can be brought together with practically no tension.

Excising the cleft. The lines A'–B'–C' are now cut through the full thickness of the lip, care being taken to keep the level of the cut on the mucosal surface identical with the skin. After the incisions have been made, any tiny line of skin attached to the vermilion near C should be carefully excised (Fig. 6).

In designing and fitting the two sides together, it is better to work with them as though working in wood, than as though they were rubber and could be pulled, stretched and molded into position. All incisions should be sharp, clear cut, definitive ones, and when the lip is opened as in swinging the triangular flap down, the cut at the angle should be complete so that the angle can fit up snugly against B on the columellar side.

At no time during the whole operation is it desirable to grasp any of the lip, which is to be used in the repair, with forceps. The gloved fingers are used for most of the holding with a somewhat clumsy appearance, but with improved healing and no forcep scratches.

Angled Crile clamps which have a soft spring are used at the corners of the mouth to help control bleeding (Fig. 6). Small mosquito forceps with rubber tubes over the jaws and a rubber band to close them gently may be substituted.

Closing the lip. A and A' are usually closed with a buried No. 000 white silk or cotton suture. If preferred, a large, firm No. 000 catgut suture is put in from the mucosal surface, picking up a good bit of tissue under both A and A' and thus in one move elevating the ala and closing the lip and nostril in the desired direction (Fig. 7).

B and B' are closed with another fine buried silk or cotton suture and with a fine surface suture. C and C' are fitted together to test the design. An excision is then made so that a V is cut out of the cleft side's vermilion just lateral to C', opening the area and dropping a V-shaped flap of the vermilion down. (This is sometimes accomplished by a single appropriate incision, simply opening the area, but this gets into the rubber idea and the "wood working" technique usually is best—Fig. 7.)

On the sound side (after being doubly sure remnants of white skin are off of the vermilion flap below C) the largest sacrifice of tissue is made. The rather long flap of vermilion is fitted across into the open vermilion cut on the cleft side and the excess is cut off. For the incisions and trimming in this region a fine, very sharp scissors is most useful (Figs. 7 and 8).

C and C' are closed with a fine surface stitch. Further surface closures are usually done between AA', BB' and CC', using fine black silk. The vermilion flaps are closed with fine surface sutures, usually anchoring the points of the flaps first. Mucosal closure is continued by going right on around the vermilion clear up the inside to the buccal fornix and being sure to close the mucosa entirely even if it rests on a raw surface of the premaxilla (Figs. 7, 8, and 9).

This mucosal closure is almost as important as the skin closure. It closes the entire lip for best primary healing and thrusts the lip forward as no other part of the operation does, by being sure there is a free loose amount of tissue below even if the upper end is tighter (Figs. 9 and 10). If this end of the wound seems too tight, it is loosened by vertical mucosal cuts on either side from the fornix downward. This is one of the few places in plastic surgery in which cutting one way and sewing another gives much help. But here the

Fig. 11. Repair of wide single cleft by method described. The normal-appearing forward-thrust of the lower portion of the lip was obtained by the use of a small flap in the lower one-third of the lip with the mucosal suturing.

soft mucosa can actually be transposed in position from a tight pursestring in the fornix to rather free flaps of mucosa that can be advanced into the lip. Complete closure of the mucosa also prevents adhesion of the lip to a raw premaxilla from occurring (Figs. 9 and 10).

This point of mucosal closure is dealt with at length because it is the point most responsible for "kicking" the lip out forward. The fine mucosal sutures put the lip where it can best stay itself. Gross stay sutures may crowd the lip forward but they will not permanently hold the tissue in place. Protrusion of the lip should be accomplished *before* stay sutures are put in.

Stay sutures of *B* black silk are put in from the mucous surface if desired, going through the lip almost to the skin, usually one or two in number.

The floor of the nose is closed with surface sutures on a small full curved needle, using the flap freed on the columellar side and any part necessary of the flap left from the incision on the cleft side. Care must be taken not to include any vermilion in the floor of the nostril where it could be seen.

The nostril can be somewhat shaped by mattress sutures through it from the skin surface to pick up the mucosa, these two surfaces having been separated during the dissection. One or two are put in the alar fold, one higher up on the ala and one to try to help form an angle at the columellar-alar junction. These sutures are not very important and can be omitted (Fig. 9).

Many operators use a mattress suture from the alar fold across the floor to tie inside the sound nostril against the septum, using small plates inside and out to prevent cutting of the sutures. If the lip is otherwise solidly closed, one can omit this suture.

The nostril is gently packed with greased gauze and a Logan bow used if desired (Fig. 18, b).

At the end of the operation, the lip should be full and in front of the lower (Fig. 10). A good flexion crease should be present. The lip should have good width and not be too long. The nostril should have a good floor, the ala should point toward the columella and the level of the ala should be the same or a little higher than the opposite one (Figs. 11 to 21).

Fig. 12. Wide total single cleft in which nasal symmetry and a full, loose lip have been obtained.

PREOPERATIVE DETERMINATIONS AND CARE

Single clefts can be repaired at any time but are preferably closed early in life. An early closure facilitates feeding, eliminates the necessity for constant apologies and explanations to friends by the parents, and the elastic pressure of the closed lip tends to narrow the anterior portion of any associated palate cleft during the first year of life. Even very young babies, if they are well developed, tolerate the operation well, and closures have been done as early as the age of 7 hours. Quite often, the father wishes to have the cleft closed before the mother sees the baby and this may be done, but one parent should see the baby beforehand. If the patient is first seen at the age of 3 or 4 days when he is losing weight, one might as well wait until he has regained his birth weight before undertaking the repair. The closure should not be done in the presence of jaundice, or in prematures or other babies weighing less than 7 pounds until they have attained that weight. Upper respiratory infections are an obvious contraindication as are any pustular skin eruptions, but small areas of uninfected "miliaria" or "heat-rash" are not.

None of these children should undergo operation immediately following a trip, but they should be under observation for 24 to 48 hours for rest and to be sure that they have not contracted any upper respiratory infection.

It is still an open question as to whether these patients might not attain better general facial development if the lip and palate closures were delayed until puberty, but other factors make this choice untenable. However, this is not "emergency surgery" and should never be done under any except the most favorable conditions. A delay of 1 month will seldom do much harm, while a satisfactory repair may be of inestimable value to the child and conversely a faulty repair may cause irreparable damage.

Feeding is always a problem in these infants and, especially if the palate is open, they are seldom able to nurse from the breast. However, it is rarely necessary to gavage them every 3 or 4 hours and an infant's esophagus will usually not stand this procedure long. They can be fed breast milk or a suitable formula with a medicine dropper or a syringe, best given with the baby held almost in a sitting position and taking from 30 to 40 minutes for each feeding rather than the usual 15 to 20 minutes.

POSTOPERATIVE CARE

No dressing is applied over the suture line when good nursing care is available (Fig.

Fig. 13. Several views of a very wide single cleft, showing small Mirault flap and forward thrust of lower portion of lip. Results shown at ages of 1 and 5 years. The usual dental deformity is seen. This can be corrected to some extent by orthodontia and limited replacement.

18, b). The nurses are instructed to clean the suture line with alkaline antiseptic solution on tiny gauze pledgets every few minutes for the first hour after operation and then every hour for the remainder of the day. After this, the lip is cleansed after each feeding and at other times when necessary to prevent the formation of any clots of blood or serum around the stitches. If experienced nursing care is not available, the suture line can be covered with a fine mesh grease gauze dressing which may be changed daily or oftener, cleansing the lip each time.

The grease-gauze pack in the nostril is removed in 48 hours, and the skin sutures on the lip are taken out on the 4th or 5th day. The Logan bow can be removed after 1 week and remaining inside sutures after 10 days.

Feedings are usually given with a syringe until 7 to 10 days after operation, after which the baby may nurse from a bottle if the holes in the nipple are burned out and enlarged. If the baby is breast fed, the breast milk is usually given with a syringe for 3 or 4 days after operation and then the baby is allowed to nurse if the palate will permit it.

Fig. 14. Extreme deformity with repair showing good alar level and good direction of the ala toward the columella.

The patient is usually discharged from the hospital on the 10th postoperative day, with the lip healed, all sutures out, no dressings, and able to nurse from a bottle or the breast, as far as the lip is concerned.

The co-operation and help of a pediatrician throughout the baby's hospitalization is solicited and gratefully received.

COMMON DEFORMITIES TO AVOID

Deformities can be seen in patients needing secondary repairs (2), and the requirements of the primary operation are thus made more clear. The patients, or their parents, are apt to focus their attention on the scar, but in many instances this is only a part of the deformity, so that the nose and lip should be studied as a whole, piecemeal, and in relation to the other features. For surgical correction, secondary deformities are often best evaluated on a "footage" basis—that is, one that can be seen across the street is worse than one which is only apparent on close inspection.

The tight, retruded lip is one of the worst and most common of the cleft lip deformities. Such lips are usually too long vertically and too narrow horizontally and are frequently the result of operating too far out from the cleft and sacrificing an unnecessary amount of substance of the lip. It is usually better to err on the side of having a full, wide lip. Even if it is a little short, this tends to improve with growth, and if not, is more amenable to secondary operations. There is practically never any great excess of tissue in a cleft lip, so that the primary excision of the cleft should involve the least possible amount to get a smooth repair.

Wide "stay-suture" scars are definitely to be avoided as they may never be entirely eliminated. It would be better to risk having the wound open up rather than put wide stay sutures on the skin surface.

Notch or "whistling deformity" of the vermilion. The more common type of whistling deformity is one in which there is a deficient amount of vermilion beneath the lip scar and it is caused by not operating far enough out laterally to get into the full thickness of vermilion on either side of the cleft. Another type is one in which the vermilion may be of almost full thickness beneath the scar but has been pulled up by the contracture of a straight-line scar. This can be prevented, in part at least, by the use of a design which will not produce a straight-line scar. Some whistling deformities have been both elements of lack of vermilion and scar pull. Excessive shortness of the mucosa may also contribute.

Tight vermilion. The mucocutaneous junction is normally a little out in front of the rest of the upper lip and retrusion or tightness of it is quite noticeable. The use of a small flap, in the operation described here, may help in obtaining a normal forward thrust of the vermilion border. Greatest difficulty may occur in the repair of partial double clefts with the open or "lazy" W type of notch. This may be due to lack of sufficient vermilion to permit fullness in this region by any design.

"Cupid's bow" in the vermilion. The slight upward prolongation of the vermilion beneath

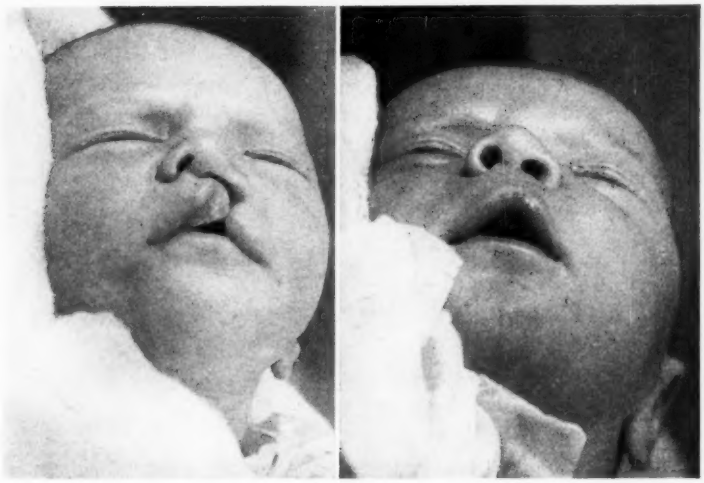

Fig. 15. Extreme soft tissue deformity with nostril on sound side just a slit. This nostril is improved in the repair, and the cleft side has a good level, but goes straight into the face instead of toward the columella.

Fig. 16. Same type of deformity as in Figure 15 with skin of lip grown down against the open alveolus, so that replacement is difficult. Alar level in the repair is good, but across the tip the ala is not open enough. Lip repair is almost normal in appearance and in muscle action.

the philtrum on either side, commonly known as a "Cupid's bow," is present in some normal lips, but almost absent in others. The desire for it, among women, seems to vary with other fashion trends.

Various operations have been proposed to create it in the cleft lip, most of them involving incisions opening up almost the entire mucocutaneous border, either at the primary operation or secondarily, and substituting a

Fig. 17. What is thought to be an excellent repair of an extreme deformity. Second view is just 6 days after operation. Later photographs at 2 years.

long scar for this normal soft undulation of tissue. It is thought that the resultant scar of these operations, in some instances, may be more deforming than the absence of the "bow." Men seem to care little for the "bow," women are apt to be undecided, and it seems too ephemeral to be the object of an operation in most instances. It can be artificially suggested by very thin areas of tattooing, or in women by the use of lipstick, without the necessity of putting a permanent scar band clear across the lip.

Disappearing vermilion. Practically no cleft lip deformity is worse than the one with disappearing vermilion, and every effort should be made to avoid it. Of chief importance, is the inside suturing and advancing mucosa forward from each buccal fornix as outlined

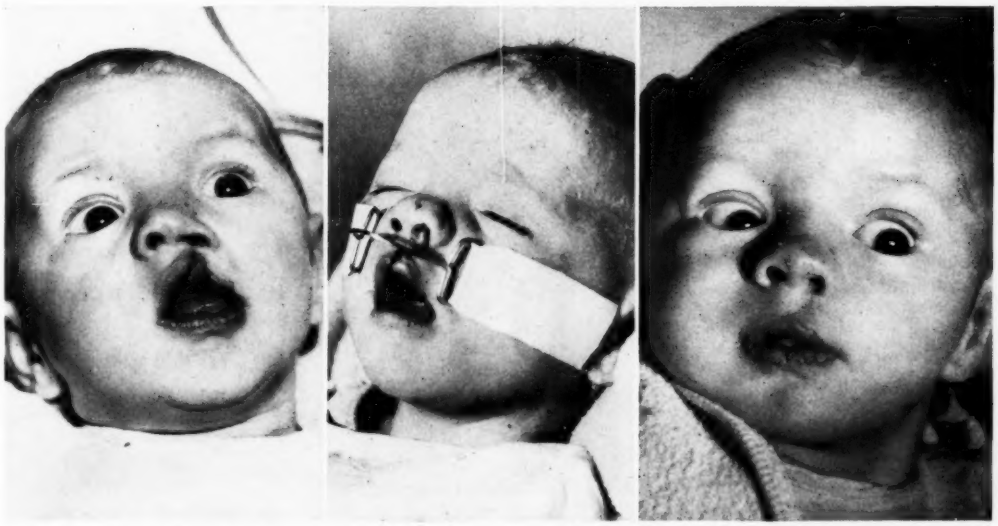

Fig. 18. Partial clefts can have all of the problems of complete clefts including those of the nose. This patient has obtained a repair that is good except for the fact that the thickness of the ala runs vertically into the face instead of starting horizontally to proceed across toward the columella.

Fig. 19. The thickness of the ala in this patient has the proper direction toward the columella. Last view is 1 week after repair.

previously. If the mucosa is carefully sutured together clear up to the nasal spine, as the last few stitches are put in, the lower border of the lip will almost invariably come forward and as it does so, the vermilion will roll out. When sutured accurately, the inside mucosa will heal by primary intention and will not become adherent to the raw premaxilla, a common cause of disappearing vermilion. The greatest difficulty is apt to come in partial double clefts with a general deficiency of vermilion.

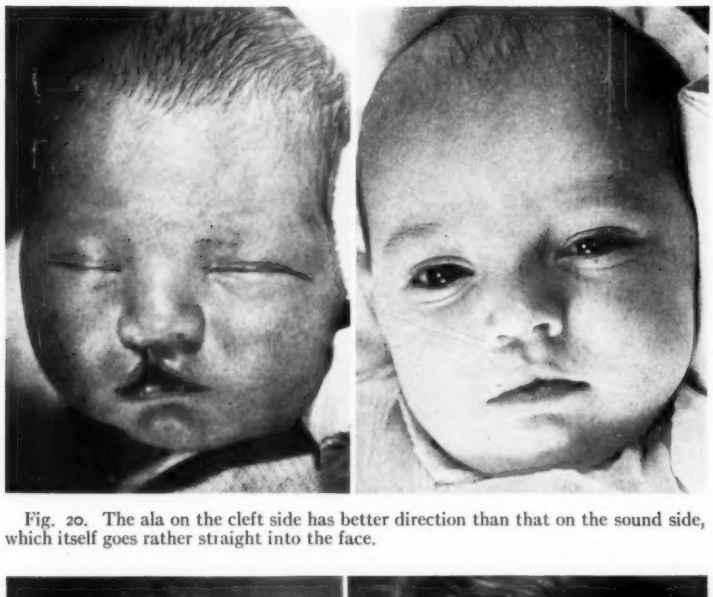

Fig. 20. The ala on the cleft side has better direction than that on the sound side, which itself goes rather straight into the face.

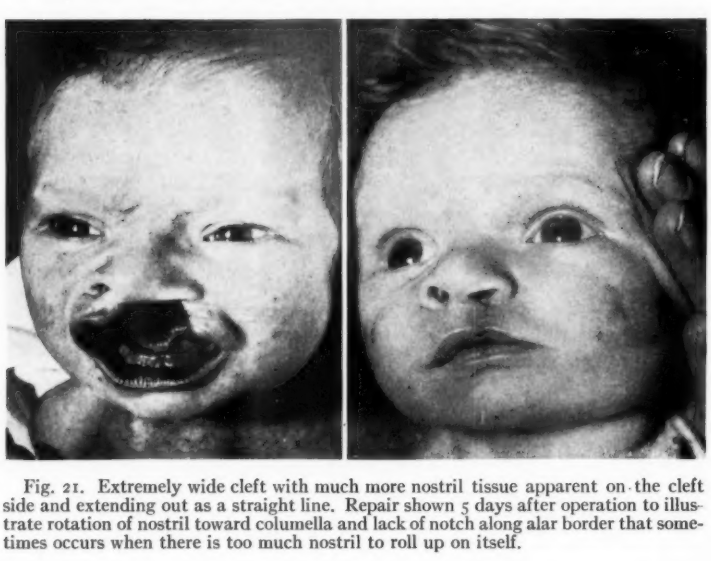

Fig. 21. Extremely wide cleft with much more nostril tissue apparent on the cleft side and extending out as a straight line. Repair shown 5 days after operation to illustrate rotation of nostril toward columella and lack of notch along alar border that sometimes occurs when there is too much nostril to roll up on itself.

Other vermilion deformities. "Stair-step" deformities of the mucocutaneous junction obviously result from inaccurate apposition of skin and mucosal edges. During the later stages of the operation, the mucocutaneous junction may be difficult to visualize so that it is quite important to mark this point on both sides of the cleft before beginning. Redundant vermilion beneath the line of the cleft is the easiest deformity to correct, but the area to be excised has to be carefully determined. Since the opposite deformity ("whistling") involves opening the whole lip for correction, it is better to err on the side of

obtaining excess vermilion in this region. Blobs of vermilion may be seen up in the skin of the lip or even in the nostril floor, at times, and represent gross mistakes in planning, or in the operation.

Excessive scar. Raised or wide scars in the line of closure may be associated with a true keloidal tendency, but are more often the result of other factors. These may be the use of heavy or wide, or tightly tied sutures, traumatizing the skin edges with forcep marks, relying on surface stitches rather than deep ones to hold the lip together, closure under excessive tension, infection, or lack of proper postoperative care to prevent crusting and its sequelae.

Depressed scars may be the result of approximating the skin with the edges slightly turned in, or of later slight separation of the skin edges while the deeper structures hold. Scars in any region may tend to become depressed so that, as a general principle of wound closure, it is probably better to finish a repair with the suture line slightly more elevated than the surrounding tissues. Depression may appear years later in a lip scar in association with an orbicularis muscle deformity.

Tattooing white scars. In rare instances, an excessively white scar may constitute the chief remaining deformity in the lip of an adolescent or adult. Injection of color directly into the scar with the finest of hand tattooing needles, as proposed by Miss Gertrude Hance, may be of distinct help. The colors should be light pastel ones and blended together beforehand to match the complexion of the patient. It is often not possible to color the scar uniformly, but if one can get enough points of color in to break the visual line of the scar, it may no longer be apparent. This coloring will not compensate for raised, keloided scars or depressed scars that form shadows in certain lights, or other irregularities in the region.

Orbicularis deformity may appear several years after a satisfactory primary repair and it is characterized by thinning of the lip and depression of the scar in the line of closure, with lumping up on either side, especially on the cleft side. A characteristic bulge in the lip is often seen just beneath the ala on the cleft side. It is thought to be associated with stretching and thinning of the union between the two sides of the orbicularis muscle as a result of excessively strong or frequent orbicularis movements or weakness in the fibrous union. This deformity may occur clear down in the vermilion, due in some instances apparently to a developmental growth or hypertrophy of a small part of the muscle.

Prominent frenulum. A large or redundant frenulum may be seen at times, in a patient with a cleft lip, upon smiling. It may be the result of not taking the mucosa of the lip loose from the alveolus at a low enough level at the time of the original mobilization, or to failure of complete mucosal healing from side to side clear up into the fornix.

Lack of nostril floor. This deformity may result either from lack of definite planning to construct a floor, or to the sacrifice of even a few millimeters of tissue in this region. This is one of the worst deformities to correct and therefore one to be especially avoided at the primary operation.

"Slumped" nostril. In a slumped nostril, the ala on the cleft side is usually displaced downward and backward and may be flared outward. Of chief importance in preventing it, is rotation of the nostril toward the columella during the primary repair (Figs. 14, 19, 20). This requires a good preliminary design, and sufficiently wide mobilization of the ala and cheek. It may be necessary to divide the nasal lining between the ala and the end of the lower turbinate to get the nostril far enough forward, but incisions that tend to encircle the nostril should be kept to a minimum. It is usually better to set the cleft ala on the same level or a little higher than the opposite one. An associated slanting of the columella may be present if the tissues on the medial side of the cleft have not been sufficiently mobilized during the primary repair. At times, this may involve elevating in the pyriform recess to get the opposite nostril up out of the face and freeing the base of the columella underneath the lip in the region of the nasal spine.

Blocked nasal airway on cleft side. The most frequent cause is lack of sufficient nasal floor so that the nostril is just collapsed. It

also may result from over-rotation of the nostril in the primary repair, or from trying to equalize the size of the two nostrils in a very wide cleft. In these latter, the actual amount of skin covering and lining may prove to be in excess of that on the normal side when measured. The nostril may extend almost straight out from the columella, and trying to roll this excessive amount of tissue into a tube, with the same amount of tissue on the small inside diameter as on the larger outside diameter, will result in a diminution in the size of the lumen. This is something like trying to roll up a thick piece of sheet rubber to make a tube rather than having it cast as a tube with a small inside and larger outside diameter.

Other nostril irregularities. In a wide cleft, the length of the nostril which is rotated to make a tube is longer than on the normal side and the cleft nostril will thus be of larger diameter than the normal one. This could probably be obviated by taking a full thickness wedge out of the cleft nostril, but seems inadvisable in an infant, and there is a tendency for some compensation of this asymmetry during growth. Corrugation of the nostril as it is rolled into a tube is lessened by undermining the skin as outlined. However, at times, there may be a remaining single notch or kink in the nostril border, usually on the lateral side near the top. This may be due to the fact that the lining cannot slip on the covering of the nostril right at the rim, as it is rotated. In such instances, one can make an incision just inside the rim and parallel to it and, by spreading with fine scissors, connect this incision with the previously undermined area. This will usually release the kink and a few carefully placed mattress sutures will help further. The incision should not be too long, as circular scars inside the nostril tend to constrict and form webs and are to be avoided. Figures 14 to 20 represent problems in nasal reconstruction, as well as details of the lip itself.

Too large Mirault flaps. A repair with a large Mirault flap (one-half the length of the lip) may be better than a straight line repair, but is not so good as when a small flap is used. It is apt to present the following disadvantages: (1) the large flaps by their greater contraction are apt to lump up more and give a "trapdoor flap" effect; (2) it is necessary to sacrifice a greater amount of lip on both the cleft and columellar sides to fashion and fit in a large flap; (3) the break in the profile line where the forward thrust begins is in the midlip rather than down just about the vermilion border where it normally occurs.

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THE SUPERIORITY OF PENICILLIN OVER BACTERIOPHAGE, SULFATHIAZOLE AND CERTAIN OTHER ANTIBACTERIAL SUBSTANCES

As Indicated by Experimental Staphylococcal Infections in Chick Embryos

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THE most important groups of bacteria from the point of view of the surgeon are and always have been, the streptococci, the staphylococci, and the gram positive sporeforming anaerobes of the gas gangrene group. It is generally recognized that the sulfonamides have taken the terror out of hemolytic streptococcal infections and have reduced the incidence of septicemia from this organism to almost negligible proportions. It was hoped that they would be equally potent against the other two groups but experience has shown that while individual cases may respond promptly and remarkably, the great proportion of cases resist sulfonamide treatment.

Our experience during the past 8 years with staphylococcal infections including septicemia has convinced the authors of the value of bacteriophage therapy in this field, particularly when clinic and laboratory work together on the problem in hand. The recent availability of penicillin has therefore led us to a study of the relative merits of these two antistaphylococcal agents both with regard to their efficacy in the treatment of staphylococcal infections and their general availability to the profession at large. We have found some clear cut evidence in the experimental data to be presented herewith.

A series of clinical and laboratory experiences with bacteriophage in staphylococcus infections has been reported by us during the last several years (3–8, 10). One of these appeared in SURGERY, GYNECOLOGY AND OBSTETRICS in 1940 (10) reporting observations made during the 2 year period from 1936 and 1938 in which 21 cases of Staphylococcus septicemia were treated, with a mortality of 28 per cent in contrast to a mortality of about 80 per cent in the previous 10 years. While our control series was not run concurrently, the results agreed closely with many other reported series. It was found that success depended upon the use of a doubly potent bacteriophage which would not only clear the turbidity of a culture of hemolytic Staphylococcus aureus but would prevent the outgrowth from a transplant from the cleared culture on a blood agar plate.

However, the production of doubly potent bacteriophage was attended with considerable difficulty in the laboratory and it was recognized that phage could not be used extensively unless a polyvalent phage of high potency could be produced commercially which would not only be doubly potent against a high percentage of infecting species but which would retain its potency over a long period of time without deterioration. The electron microscopic picture of bacteriophage as shown by Luria suggested quite clearly that phage is a living ultramicroscopic body requiring certain very definite conditions under which it might be expected to survive. Our clinical and laboratory experience with the available commercial phages agreed with reports which were obtained from other sources that they were not dependable.

The search for a method whereby a clear cut appraisal of the value of these two and certain other antistaphylococcal agents might be obtained, led us to a consideration of the experimental infection of embryonated hens' eggs.

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T. and M. Rakieten were the first to study the action of bacteriophage in developing chick embryos. They used dysentery phages and succeeded in saving the embryos with the bacteriophage given as long as 5 hours following the injection of the bacteria. The majority of the embryos which survived the experimental period of 6 days proved to be free of bacteria and phage was found to have propagated in the medium.

MacNeal, Blevins, and Pacis, using dysentery phage, obtained essentially the same results. Green and Birkeland employed the embryonated eggs for the study of the effect of phenol, iodine, and cetyl pyridinium chloride (ceepryn) on infection produced by Staphylococcus aureus. They found that ceepryn had definite curative effects, while phenol and iodine failed.

In addition to bacteriophage and penicillin, we have also appraised sulfathiazole, ceepryn, phemerol, chinosole, antistaphylococcus serum (type A Julianelle of Lederle) and staphylococcus antitoxin (of Lederle).

Among the newly discovered agents we have studied: carboxymethoxylamine (CMOA) obtained from Dr. E. J. Pulaski, of this laboratory, "vioform" (Ciba), and the concentrated extract made from the filtrate produced by a gram positive aerobic sporulating bacillus which has strong antibiotic activity discovered by B. A. Johnson of this laboratory.

TECHNIQUE

Ten day old embryonated eggs were used. The injections of the tested substances were made into the allantoic sac at the edge of the chorioallantoic membrane, avoiding the larger vessels. This was done through a small hole made with an egg piercer. In order to relieve pressure within the egg and to allow a free passage of fluid, another small hole was drilled into the air sac. After the inoculation both holes were sealed with surgical Scotch tape. The inoculated eggs were kept in the incubators at 38.5 to 39.5 degrees C.

Simultaneously with the egg inoculations, analogous inoculations were made into 25 cubic centimeter savita broth tubes, and these were observed for the duration of the egg experiment.

All dead eggs were immediately dissected. The cultures of the egg fluid material and of the heart of larger embryos were made on blood agar plates and broth. In a majority of the experiments, the eggs which survived 7 day periods after the inoculation, were killed by chilling for 1 hour in the refrigerator and then were dissected and cultured.

In some experiments the eggs were left in the incubator for hatching. The unhealthy chicks which hatched were sacrificed and cultured. The healthy ones were bled from a large peripheral vein for cultures and allowed to grow.

Our experiments were carried out with two strains of Staphylococcus aureus. Strain B was isolated from a furuncle and strain D from the blood stream of a patient.

We found that 0.1 cubic centimeter of a 5 hour savita broth culture of both strains, containing between 150 to 200 million bacteria, consistently killed a 10 day old chick embryo within 24 hours. This amount was therefore used as the test dose.

The injections of 0.1 cubic centimeter of a dilution 10^{-1}, 10^{-2}, and 10^{-3} were also fatal, but the embryo died between 1 and 5 days thus making it unsuitable for use as the test dose.

The savita broth cultures were made from blood agar slants which were inoculated directly with the egg material of the culture control egg of the previous experiment.

The bacteriophage employed was our stock staphylococcus mixture. With a titer of 10^{9}, 0.1 cubic centimeter of this phage produced complete visible lysis of 0.1 cubic centimeter of each of two strains of staphylococci when set in 25 cubic centimeters savita broth. (The amount equivalent to the fluid content of an egg.) However, a few degenerated colonies often appeared on the blood agar plates, and a visible secondary growth was usually seen after 1 week of incubation. This does not fulfill the criteria of "double potency" although "doubly potent" phage could always be obtained with bacterial inoculations of 0.25 to 0.75 cubic centimeters instead of 0.1 cubic centimeter; or when 0.1 cubic centimeter of the 10^{-1} dilution of phage was added to 0.1 cubic centimeter bacterial inoculum,—the optimal concentration for lysis and the propaga-

TABLE I.—THE EFFECT OF STAPHYLOCOCCUS BACTERIOPHAGE ALONE AND IN COMBINATION WITH CEEPRYN AND PHEMEROL AS COMPARED WITH PENICILLIN ON THE CONTROL OF EXPERIMENTAL STAPHYLOCOCCAL INFECTION IN EMBRYONATED EGGS

Substances inoculated	Number of eggs	Death in 24 hours	Cultures		Dead 2–4 days	Culture		Dead 5–7 days	Culture		Lived 7 days or more	Culture		% of eggs survived 7 days or more	% of eggs which were free of growth
			Sterile	Growth		Sterile	Growth		Sterile	Growth		Sterile	Growth		
Culture alone	32	30	—	30	2	—	2	—	—	—	—	—	—	—	—
Culture+phage	19	—	—	—	7	—	7	6	1	5	6	1	5	31	10.5
Culture+phage+ceepryn	17	—	—	—	6	1	5	5	1	4	6	—	6	35	11.7
Culture+ceepryn	4	2	—	2	2	—	2	—	—	—	—	—	—	—	—
Culture+phage+phemerol	15	2	—	2	4	1	3	3	—	3	6	1	5	40	13.3
Culture+phemerol	4	1	—	1	3	—	3	—	—	—	—	—	—	—	—
Culture+penicillin	50	2	1	1	2	1	1	14	10	4	32	29	3	64	82

tion of phage being in that ratio of phage corpuscles to bacterial bodies. But such a mixture was not suitable for inoculation into the eggs.

The majority of penicillin experiments were carried out with the calcium salt of penicillin manufactured by Pfizer. This was dissolved in physiological saline in concentrations of 5000 and 1000 units per cubic centimeters and kept frozen in dry ice.

RESULTS

The results with staphylococcus phage. In this series of experiments, bacteriophage was injected into most of the eggs immediately following the inoculation of bacteria. Some were inoculated 1 hour after the bacteria.

A group of eggs was also inoculated with bacteriophage and bacteria mixed in the test tube prior to the egg inoculation. Of the 19 eggs, inoculated with bacteriophage immediately following the inoculation of bacteria, no eggs succumbed within 24 hours while the control eggs, inoculated with bacteria alone all died. Six eggs lived more than 7 days. Several others survived for 2 to 7 days. Thus the injection of phage immediately after the culture resulted definitely in prolonging the life of the infected chick embryos (Table I).

Almost identical results were obtained in 12 eggs with a mixture of bacteria and bacteriophage made prior to the egg inoculation and in four eggs inoculated 1 hour following the inoculation of bacteria.

Culture of the egg material of all phage-treated embryonated eggs yielded, with two exceptions, some growth of staphylococci. The amount of growth was always greatly diminished as compared with culture controls. In some cases only a few colonies developed. However, we noticed no consistent correlation between the duration of life of the embryo and the amount of bacterial growth. The signs of phage action on the culture, such as loss of pigmentation of the colonies, fragmentary and degenerated colonies, the presence of phage plaques, etc., were always in evidence. Fished colonies which grew in savita were as susceptible to phage as the original culture. The cultures of the egg material, as a rule, displayed a greater effect of bacteriophage than did the cultures of the blood of the embryos, but it was evident that bacteriophage together with bacteria entered the blood stream of the infected embryo and maintained itself there. Bacteriophage recovered from the egg material of the phage-treated eggs, possessed varying degrees of lytic power. In some cases it was able to produce a complete visible lysis of the homologous and of certain heterologous strains of staphylococci. The lytic ability of these phages in savita broth and the degree of colony destruction on the blood agar was always greater than that of the phages which were recovered from the heart of the embryos. Furthermore, the titration of egg material in many instances revealed a return of the bacteriophage corpuscular count to the original level and somewhat above this level.

In other cases there were various degrees of diminution of the bacteriophage titer. In a few specimens no phage could be recovered by

the ordinary laboratory methods. Decrease of phage titer and its complete disappearance were especially characteristic of the specimens of egg material stained with blood.

We found no consistent correlation between the potency of bacteriophage isolated from egg material (as estimated by its lytic power and its titer) and the duration of life of the infected embryonated eggs. In order to obtain clearer evidence of the ability of bacteriophage to proliferate in the embryonated eggs, some eggs were inoculated with various dilutions of bacteriophage.

Tenth cubic centimeter amounts of the 10^{-2}, 10^{-4}, 10^{-5}, and 10^{-6} dilutions were used together with susceptible bacteria. The multiplication of bacteriophage was observed with dilutions 10^{-2} and 10^{-4} and not with dilutions 10^{-5} and 10^{-6}. In one of these experiments no multiplication of the phage took place even with dilutions 10^{-2} and 10^{-4}, while the undiluted phage decreased in titer. Thus, apparently the chorioallantoic fluid possessed some ability to destroy or neutralize staphylococcus bacteriophage. The degree of destruction varied in different eggs. However, if a sufficiently large dose of undiluted phage was used, that is 0.1 cubic centimeter, multiplication of phage occurred in the majority of cases.

In vitro results with chorioallantoic fluid. In view of the variability in the fate of bacteriophage in different embryonated eggs and the inhibiting effect of the blood of some of the embryos we felt that certain *in vitro* experiments had to be carried out.

For this purpose three specimens of clear chorioallantoic fluid with and without the homologous blood, three specimens of mixed egg fluid with and without blood, and three specimens of human serum were used. All specimens were tested undiluted, and in dilutions of 1:2, 1:10, 1:20, 1:50, 1:100, and 1:200. The titrations of the undiluted and the 1:2 dilutions of each specimen were carried out. We found that complete visible clearing occurred in 1:10 and all higher dilutions of all specimens of chorioallantoic fluid, and a partial lysis in undiluted and 1:2 dilutions.

In the presence of blood, complete clearing occurred in dilutions of 1:50 or higher, with only partial clearing in the lower dilutions.

The titration of the phage in the undiluted and in the 1:2 dilution of chorioallantoic fluid and of the mixed egg fluid material in all but one specimen revealed a definite propagation of bacteriophage to its original level of 10^9. There was no difference in the titer, whether the specimens contained or were free from blood. This titer was equivalent to that of the phage control, propagated in savita broth, but the titer of phage propagated in the undiluted and in the 1:2 dilution of the human sera decreased 10 to 100 times. Thus, it is apparent that bacteriophage is capable of multiplying and producing lysis of some bacteria in the presence of chorioallantoic fluid and of other fluid constituents of the embryonated eggs.

The combined effect of staphylococcus phage with phemerol and ceepryn. From previous *in vitro* experiments with phemerol, ceepryn, xephiran, and chinosol, we found that phemerol in a dilution of 1:1 million and ceepryn in a dilution of 1:10 million exerted little or no deleterious effect on staphylococcus phage. At the same time they possessed a significant bacteriocidal effect on staphylococci and other gram positive organisms. It was frequently observed that the combination of phage with phemerol or ceepryn produced a complete destruction of bacterial suspensions, an effect which neither agent could alone produce. We found that zephiran in a dilution of 1:50,000 which was recommended by E. Maier as a bacteriophage preservative, definitely cut down the titer, and the lytic power of staphylococcus bacteriophage. The same was found true for chinosol (1) widely used as a preservative in Russia.

On the basis of these findings, a series of embryonated eggs were inoculated with staphylococci and treated with ceepryn and phemerol alone and in combination with bacteriophage. The injections were carried out immediately following or 1 hour after the inoculation of bacteria.

The results of the combined treatment are presented in Table I and are essentially the same as those obtained with bacteriophage alone. There was a prolongation of life of the chick embryos,—but the majority of the cultures of the egg material revealed sparse phage-contaminated growth. Ceepryn and

TABLE II.—EFFECT OF CALCIUM SALT OF PENICILLIN (PFIZER) ON STAPHYLOCOCCUS INFECTIONS IN EMBRYONATED CHICK EMBRYOS

Number of eggs	Interval between bacteria+ penicillin	Dead 1–3 days	Culture		Dead 4–7 days	Culture		Lived 7 days or more	Culture	
			Sterile	Growth		Sterile	Growth		Sterile	Growth
50	Immediately	4	2	2	14	10	4	32	29	3
8	15 minutes	—	—	—	—	—	—	8	5	3
10	1 hour	2	1	1	1	—	1	7	6	1
10	2 hours	1	1	—	2	—	2	7	6	1
4	3 hours	—	—	—	—	—	—	4	4	—
6	4 hours	2	—	2	—	—	—	4	3	1
4	5 hours	1	1	—	—	—	—	3	2	1
4	6 hours	2	1	1	—	—	—	2	2	—
Totals 96		12	6	6	17	10	7	67	57	10

Survival over 7 day period 70%
Complete sterilization of culture 76%

phemerol alone, were less effective (Table I).

The effect of the combined treatment of phage with ceepryn or phemerol, given 1 hour following the inoculation was similar to that obtained when these substances were given immediately following the bacterial inoculations.

The injection of 1 per cent chinosol (hydroxyquinoline sulfate) immediately following the inoculation of bacteria produced a sterilizing effect on staphylococci in the egg, but it was toxic to the embryos and killed them within 24 hours.

The results with penicillin. The injections of different eggs were made at varying intervals following the inoculation of bacteria. Some eggs received penicillin immediately after the bacteria, others after 15 minutes, 1 hour, 2 hours, 3 hours, 4 hours, 5 hours, and some 6 hours following the bacteria. Doses of 0.1 cubic centimeter of penicillin containing 500 units, 100 units, 10 units, and 1 unit were used.

The results of the experiments on the effect of the calcium salt of penicillin of Pfizer is presented in Table II. From this chart one can see that 96 embryonated eggs were injected with 100 units of penicillin immediately and up to 6 hours following the inoculation of bacteria. Sixty-seven of these 96 eggs, that is 69 per cent, survived a 7 day experimental period. Of these 57, or 85 per cent, did not yield any growth on the culture. Sixteen more eggs of the 29 which died within the experimental period were found free of growth. The cultures of the eggs inoculated with penicillin were made in plain broth and on blood agar plates in the presence of clarase (9).

In those instances in which the growth of staphylococci persisted, it was rarely as abundant as in the culture controls and the colonies looked degenerated. There was no significant difference in the outcome of the penicillin therapy when it was given immediately following the inoculation of bacteria or within a 6 hour period. These experiments must be repeated with still longer intervals up to 24 hours.

Thus the injection of 100 units of penicillin exerted a definite protective effect on the infected chick embryos. It was often capable of destroying all of the inoculated bacteria. And even in those eggs in which the sterilization was incomplete, penicillin prolonged the life of the chick embryos. It also allowed hatching of some of the eggs, which were incubated over the 7 day experimental period.

Table III shows the therapeutic and sterilizing effect of 100 units, 10 units, and of 1 unit of penicillin. In this experiment the injections of penicillin were made immediately following the inoculation of bacteria or within a 4 hour period. Once again there was no significant difference in the protective power when 100 units or 10 units of penicillin were given but the protective power of 1 unit was lower. However, there was a marked difference in the bactericidal effect of different amounts of penicillin when cultures were made, 100 units

TABLE III.—COMPARATIVE THERAPEUTIC EFFECT OF 100 UNITS, 10 UNITS AND OF 1 UNIT OF PENICILLIN (CALCIUM SALT-PFIZER) ADMINISTERED IMMEDIATELY AFTER 1 HOUR, 2 HOURS, AND 4 HOURS FOLLOWING THE ADMINISTRATION OF BACTERIA

Number of units	Interval between bacteria & penicillin	Number of eggs	Dead 1–3 days	Culture		Dead 4–7 days	Culture		Lived 7 days or more	Culture			
				Sterile	Growth		Sterile	Growth		Sterile	Growth		
100	Immediately	6	—	—	—	2	1	1	4	4	—		
10	Immediately	4	—	—	—	—	—	—	4	2	2		
1	Immediately	4	1	—	1	1	—	1	2	—	2		
100	1 hour	10	2	1	1	1	—	1	7	6	1		
10	1 hour	7	3	2	1	—	—	—	4	3	1		
1	1 hour	4	1	—	1	2	—	2	1	—	1		
100	2 hours	10	1	1	—	2	—	2	7	6	1		
10	2 hours	7	1	—	1	2	—	2	4	—	4		
1	2 hours	4	2	1	1	1	—	1	1	—	1		
100	4 hours	6	2	—	2	—	—	—	4	3	1	% of eggs survived 7 days or more	% of sterile cultures
10	4 hours	4	2	—	2	—	—	—	2	1	1		
1	4 hours	3	2	—	2	—	—	—	1	—	1		
100	Total	32	5	2	3	5	1	4	22	19	3	69	69
10	Total	22	6	2	4	2	—	2	14	6	8	64	36
1	Total	15	6	1	5	4	—	4	5	—	5	33	7

of penicillin sterilized 19 out of 32 eggs, 68 per cent; 10 units of penicillin sterilized only 8 out of 22 eggs, 36 per cent; 1 unit of penicillin failed to sterilize a single egg that lived longer than the 7 day experimental period.

Analogous experiments carried out with 100 units, 10 units, and 1 unit of penicillin in 25 cubic centimeters of savita broth revealed the following: Both 100 units and 10 units of penicillin produced a very marked bactericidal effect on staphylococci and frequently produced the destruction of all bacteria. In some experiments, however, a few bacteria survived the whole 7 to 12 day period of incubation. During this time the savita broth remained clear, and the presence of bacteria could be revealed only by inoculating blood agar plates. One unit of penicillin also possessed a significant bactericidal power in the savita broth which was clear after 24 hours of incubation, but it usually showed growth after 72 hours of incubation.

The injection of 500 units of penicillin proved to be toxic for some of the eggs. And although 3 out of 9 eggs survived for 6 or more days, 6 others, including 3 controls, inoculated with penicillin alone perished within 2 days.

OTHER BACTERIOSTATIC AGENTS

Sulfathiazole (*ST*) was used in a concentration of 285 milligrams per cent (the highest concentration possible in water). One-tenth to two-tenths cubic centimeter of the drug were administered immediately following the injection of staphylococci. No significant beneficial effect was observed, as all chick embryos died within 4 days. The culture of the egg material showed some diminution and a marked degeneration of the bacterial growth. Similar results were obtained with the combined administration of bacteriophage and sulfathiazole in 6 infected eggs. Among 3 control eggs, inoculated with 0.2 cubic centimeter of sulfathiazole alone, 2 died within 3 days, while 1 lived for 5 days.

Thus the results seem to indicate the lack of beneficial effect and an apparent toxicity with this concentration of the drug for the chick embryo.

The experiments *in vitro* demonstrated that 0.2 cubic centimeter (containing 57 mgm. of ST) produced only a partial inhibitory effect against 0.1 cubic centimeter of the culture (150–200 million bacteria) in 25 cubic centimeter savita broth. The inhibition of bacteria was complete when a small number of staphylococci ranging between 15,000 to 150,000 of bacteria were tested. So that we feel that if the standard bacterial inoculum would be decreased, the effect of the drug might have been more manifest.

Antistaphylococcus rabbit serum (*Julianelle*) *and staphylococcus antitoxin* (*horse serum—Lederle alone and in combination with bacteriophage*).

The administration of serum in 0.1 cubic centimeter to 0.2 cubic centimeter amounts was made immediately following the inoculation of bacteria.

Both substances produced some prolongation in the life of the embryos, but none lived longer than 7 days.

Cultures of the egg material of the serum treated eggs, did not reveal any significant diminution in the amount of growth as compared with the culture controls, and there was no apparent degeneration of the colonies.

Both types of sera exerted a slight inhibiting effect *in vitro*.

Carboxymethoxylamine (*CMOA*) immediately following the inoculation of bacteria resulted in a slight prolongation of life of the embryos. The drug also produced a complete destruction of all bacteria in some of the infected eggs. However, it was obviously toxic, having killed all the 4 control eggs within 2 days. It was interesting to note, that having possessed a considerable bactericidal effect, CMOA did not reduce the titer of bacteriophage or interfere with its proliferation when used concurrently. The marked bactericidal effect of CMOA and its harmlessness for bacteriophage were confirmed *in vitro*.

Vioform (*Ciba*) was employed in concentrations ranging between 1:200 and 1:500,000, 0.1 cubic centimeter of these dilutions being administered immediately after the bacteria. No protective or bacteriostatic effect was observed with this agent *in vivo*, and there was no significant inhibiting action *in vitro*. In concentration of 1:200 vioform was not toxic for the embryos.

B. A. Johnson's Bacillus T (*antibiotic*). The filtrate from a 3 day culture of this organism in various media is nontoxic for animals and has a strong bacteriostatic action *in vitro* against all of the gram positive organisms with which it has been tested. It may be concentrated by a number of methods which will be reported elsewhere. The substance used in these experiments was a crude concentrate containing about 100 units per cubic centimeter. It proved to be efficacious in prolonging the life of the embryos but was not as good as penicillin. Three out of 4 injected eggs survived the 7 day experimental period and one of these hatched. However, the cultures showed only a partial inhibition of the growth and there was invasion of the blood stream.

The chick which hatched revealed the presence of bacteria in the absorbed yolk sac,—but there was no invasion of the blood stream.

SUMMARY

1. The inoculation of the chorioallantoic fluid of 10 day old chick embryos with 0.1 of a savita broth culture of Staphylococcus aureus consistently brought about the death of the embryos within 24 hours.

2. The administration of staphylococcus bacteriophage immediately following the inoculation of bacteria, prolonged the life of all chick embryos.

3. The cultures of the egg material of the phage-treated embryonated eggs resulted in a decrease and a degeneration of bacterial growth. However, a complete sterilization was seldom achieved.

4. The presence of bacteriophage in the chorioallantoic fluid usually did not prevent the bacterial invasion of the blood stream of the embryos, although the appearance of phage in the blood usually could be demonstrated.

5. Active multiplication of bacteriophage occurred in the majority of the cases when the undiluted or lower dilutions of phage were used. But dilutions of 10^{-5} or higher seldom multiplied and often completely disappeared.

6. The *in vitro* experiments carried out with chorioallantoic fluid and with a mixture of the egg material showed that staphylococcus phage not only multiplied in these fluids but also produced a lysis of susceptible bacteria suspended in them. The presence of embryonic blood did not prevent bacterial lysis, although there was some inhibition.

7. The addition of ceepryn or phemerol did not significantly change the therapeutic results of bacteriophage treatment of the infected embryonated eggs.

8. The administration of 100 units of the calcium salt of penicillin anytime within 6 hours following the bacterial inoculation resulted in survival of the majority of the embryonated eggs for the 7 day experimental period and in hatching of eggs when incubation was prolonged beyond this period.

9. The therapeutic results were essentially the same when 10 units of penicillin was administered but survivals fell off when 1 unit was used.

10. The sterilization of the infected eggs, however, depended upon the numbers of units of penicillin used. A complete sterilization occurred in 76 per cent of all eggs inoculated with 100 units of penicillin.

11. The administration of 28.5 or 57 milligrams of sulfathiazole simultaneously with the bacteria failed to prolong the life of the embryonated eggs or to produce significant bacterial inhibition of the test dose.

12. Antistaphylococcus rabbit serum (Julianelle) and staphylococcus antitoxin horse serum in 0.1 and 0.2 cubic centimeter amounts produced some prolongation of the life of the

eggs, but the antibacterial effect of these substances was also insignificant.

13. Carboxymethoxylamine (CMOA) tested in 0.5 per cent concentration produced a sterilizing effect *in vivo* and *in vitro* in a majority of the cases, but was found toxic for the embryos. Only the local use of this drug can be considered safe.

14. Vioform in 0.5 per cent concentration was not toxic but possessed only a slight bacteriostatic effect.

15. The new antibiotic agent, discovered by Miss B. Johnson from Bacillus T, a gram positive sporulating bacillus, exerted a significant protective effect of the embryos, but in the concentrations which were used it was not as efficient as penicillin.

CONCLUSIONS

1. Penicillin is outstanding in saving chick embryos or prolonging life when inoculated with virulent hemolytic Staphylococcus aureus cultures, in doses which regularly kill controls in 24 hours. In this respect it is superior to staphylococcus bacteriophage or staphylococcus antitoxin or vioform, or carboxymethoxylamine or sulfathiazole, or another antibiotic derived from Bacillus T.

2. The increasing availability of penicillin and its demonstrated efficiency in the clinical treatment of staphylococcus infections relegates the use of staphylococcus bacteriophage in these infections to a place of second rank and only to be considered in cases in which penicillin fails.

3. Our efforts to produce a more highly potent staphylococcus phage by the use of egg embryos has not been successful. The difficulties of developing a commercial phage of high potency and prolonged activity still remain.

4. Further studies are indicated in the field of antibiotics for the staphylococcus and other organisms.

5. Egg embryos offer a reliable medium for the appraisal of antistaphylococcus agents and other antibacterial substances.

During the writing of the present publication, a paper by Green and Birkeland has appeared in the *Journal of Infectious Diseases*, 1944, 74: 32. Among various wound antiseptics the authors studied the effect of penicillin, ceepryn, and phemerol. The results obtained by these authors with penicillin are similar to ours. Ceepryn and phemerol were used in much higher concentrations and were found to be effective sterilizing agents.

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EXPERIMENTAL STUDIES OF PERIPHERAL NERVE INJURIES

III. A Study of Recovery of Function Following Repair by End to End Sutures and Nerve Grafts

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A STUDY was made of the recovery of function following section of peripheral nerves by a razor blade and gunshots and repair by end-to-end sutures and nerve grafts.

The experiments were performed upon 470 cats and the nerve involved was the sciatic. Procedures were standardized so that two surgeons performed all the operations and followed the same methods and technique. Identical methods of clinical examination were used by two examiners.

OPERATIVE PROCEDURES

Following induction by intravenous nembutal anesthesia (nembutal gr. 0.2 per pound of weight), the animal was tied to a board with the hind legs in extension at the hips and slightly flexed at the knees. The external aspect of the left thigh was shaved, the skin prepared with iodine and alcohol and draped. The entire operative procedure was done under strict asepsis. A 6 centimeter long incision was made parallel to the femur on the posterior surface of the thigh, its upper end reaching a point half way between the tuberosity of the ischium and the greater trochanter. The skin and subcutaneous tissue were retracted and the line of cleavage between the biceps femoris and the vastus lateralis muscles was exposed. These muscles were retracted from each other, thus exposing the caudofemoral, the lower border of the gluteus maximus, the lateral surfaces of the abductor femoris and semimembranous muscles, the fat of the popliteal space, and the sciatic nerve in its entire course in the thigh from the level where it gives off branches to the hamstring muscles to a point below its division into the tibial and common peroneal nerves. The length of nerve exposed averaged 6 centimeters. Section of the nerve with a razor blade and repair were performed in its proximal half.

A detailed description of the technique used to obtain uniform experimental gunshot nerve injuries was given in a previous article.

A. Sharp Section Experiments

End-to-end sutures were performed in 34 animals. After exposure the sciatic nerve was lifted from its bed and sectioned with a razor blade at a point about 3 centimeters above its division or 1 centimeter from the point where it usually disappears beneath the caudofemoral muscle. The sectioned ends of the nerve were accurately approximated by five to six sutures uniting their epineural sheaths. The sutures employed were a single untwisted strand of black twisted Champion surgeon's silk No. 4. The nerve was not sutured until all epineural and perineural bleeding had stopped, and special care was taken to suture only the epineurium. The nerve bed was kept moist with saline solution during the operation. The fascia of the biceps femoris and vastus lateralis muscles was approximated with one or two silk sutures, and the skin was closed with clips. The wounds healed without infection and the clips were removed on the 10th postoperative day. No dressings were applied and the leg was not immobilized.

Autogenous grafts were performed in 85 animals. A piece of the exposed sciatic nerve measuring from 2.0 to 2.5 centimeters was re-

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sected and resutured into its previous position without taking special care in the approximation of the cross section fascicular pattern of the nerve. The graft was frequently rotated. Five to six silk sutures approximated the epineurium of the graft to the epineurium of the proximal and distal nerve segments. The distal suture line was situated approximately 1.5 centimeters above the division of the sciatic nerve.

Homogenous grafts were performed in 71 animals. The graft, measuring from 2.0 to 2.5 centimeters, was taken from the sciatic nerve of another cat and sutured into a gap produced by the resection of a nerve segment of equal length. The ends of the graft were approximated by 5 to 6 epineural sutures to the proximal and distal nerve segments without paying particular attention to the cross section fascicular arrangements of the nerve. The homogenous grafts were usually transplanted immediately after they were obtained; in a few cases they were kept in sterile saline solution for 24 hours and in 8 animals the grafts were preserved for various periods in 2 per cent, 50 per cent, and 70 per cent alcohol before transplantation.

Following end-to-end suture the repaired nerves were removed after a period of 30, 45, or 60 days. In a large number of autogenous and homogenous grafts the distal suture line was resected for a length of 0.5 to 1.0 centimeter, depending upon the amount of scar and the mass of neuroma present 45, 60, or 75 days after implantation of the graft, and a new distal suture was performed. The repaired nerve was removed another 45, 60, or 75 days later, or 90, 120, and 150 days after primary implantation of the graft.

At autopsy the entire sciatic nerve was removed including its tibial and peroneal divisions as far as the ankle. The specimen was suspended on glass rods and fixed in a 10 per cent formalin solution and imbedded in paraffin. Serial longitudinal and cross sections of the specimen above and below the point of repair and of the graft were stained to show the connective tissue, myelin sheaths, and nerve fibers according to the van Gieson, Weil, Bodian, sudan III, silver pyridine, and Bodian-fuchsin methods.

ANATOMICAL APPEARANCE OF THE REPAIRED NERVES

a. End-to-end sutures. The gross appearance of the nerve and suture lines was about the same 30, 45, and 60 days after repair. In most of them a few thin adhesions were present between the suture line and the surrounding tissue, in which numerous small blood vessels could be seen. The adhesions were never severe enough to immobilize the nerve or to fix it to one of the surrounding muscles. Usually a slight swelling was observed at the suture line on which the black silk sutures could be seen (Fig. 1).

b. Autogenous grafts. The grafts usually appeared to be thicker and more voluminous at the time of removal than at the time of implantation and were also thicker than the proximal and distal nerve segments to which they were sutured. The proximal suture line was usually slightly swollen, and the distal suture line showed in most cases a medium amount of swelling 45, 60, and 75 days after implantation of the graft. This swelling of the second distal suture line seemed to be smaller an equal number of days after the primary distal suture line had been resected and resutured. Well formed blood vessels could always be observed in the epineurium of the graft, penetrating the epineurium at the distal suture line and traveling toward the proximal suture line. A small amount of thin adhesions were also present around the suture lines and the graft, but generally did not immobilize the nerve. These adhesions carried numerous blood vessels including those which were seen in the epineurium (Fig. 2).

c. Homogenous grafts. The anatomical appearance of these grafts differed from that of the autogenous grafts in so far as they were thicker, more voluminous, had a fusiform shape, and gave the macroscopic impression of a neuromatous mass (Fig. 3). Both suture lines were swollen, the distal more than the proximal. Larger amounts of adhesions surrounded the graft and connected it with the surrounding tissues and frequently small muscle bundles were attached to the thickened epineurium and immobilized the graft. The adhesions were always very vascular, and numerous blood vessels could be seen entering

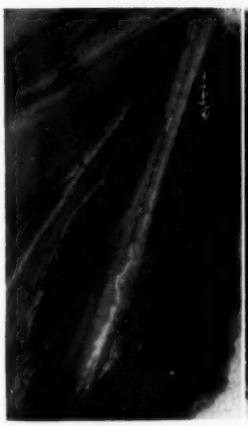

Fig. 1.

Fig. 2.

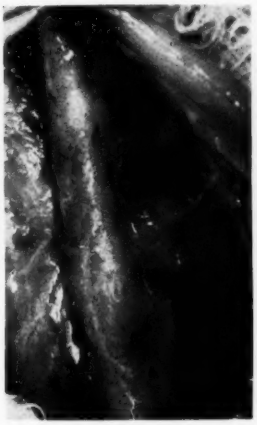

Fig. 3.

Fig. 1. Sixty days after end-to-end suture of the left sciatic nerve. There is a slight swelling of the suture line but no apparent adhesions between the nerve and the surrounding tissue.

Fig. 2. Autogenous graft 120 days after transplantation into the left sciatic nerve. A slight swelling of both suture lines is present; silk sutures are visible at the site of the distal suture. There are a few adhesions between the graft and the surrounding tissue. Small blood vessels can be seen in the epineurium of the graft.

Fig. 3. Homogenous graft 75 days after transplantation into the left sciatic nerve. The graft is spindle shaped and thicker than the proximal and distal nerve segments. The swelling of the suture line is more marked distally. Strands of adhesions are present between the graft, the suture lines and the surrounding muscles.

the epineurium of the graft. When the graft was freed from its adhesions, the surface of the thickened epineurium was usually covered with minute drops of blood. In a few cases in which a large swelling of the proximal suture line was always present, the graft remained thin, had a fibrotic appearance, and a hard and stringy consistency, and the distal suture line was only slightly swollen.

A few alcohol stored homogenous grafts have been used, and they differed from the other fresh homogenous grafts by their pale and more fibrotic appearance and only a few small scattered vessels were present in the epineurium. They were also surrounded by poorly vascularized adhesions and the suture lines were equally swollen.

After resection and resuture of the distal suture line, new adhesions formed between the suture line and the surrounding tissue. The secondary suture line was generally smaller than the resected one, but some swelling was always present. In animals which were allowed to live for longer periods of time, up to 33 months, the grafts appeared to be of the same size as the proximal and distal nerve segments, and the suture lines were often indistinguishable from the graft and the rest of the nerve. The adhesions were usually very thin, and the graft as a whole did not differ from a normal nerve. This was particularly true of the autogenous grafts. The epineurium of the homogenous grafts was never as smooth and transparent as that of the autogenous grafts or the normal nerves.

MICROSCOPIC STUDIES

Depending on the age of the specimen the serially sectioned and stained nerve and graft specimens showed various signs of degeneration and regeneration.

Although the nerves were sectioned with a sharp razor blade and repaired by delicate suturing of the epineural sheaths with fine silk, the site of section and repair always showed a traumatic zone within a few millimeters of the two ends. This area was characterized by a breaking down of the myelin, edema, and an accumulation of débris between the endoneural tubes in place of the

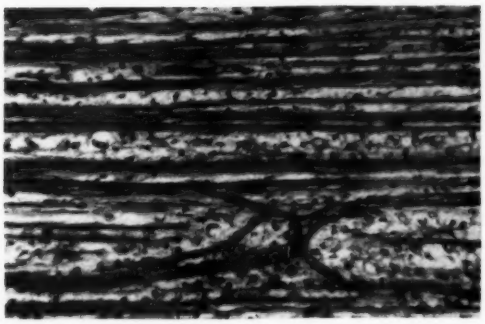

Fig. 4. Distal segment of the left sciatic nerve 30 days after end-to-end suture. The endoneural tubes are filled with myelin decomposition products and a large number of gitter cells is present especially around the capillaries. Regenerating nerve fibers follow the endoneurium which shows a cellular proliferation. (Bodian-fuchsin stain, × 170.)

original myelin sheaths. The axis cylinders also underwent degenerative changes and finally broke down completely. The trauma led within a few days to a proliferative reaction of the endoneurium in the end of the proximal segment, which resulted in structural obliteration of the original endoneural tubes and was accompanied by disturbances in the removal of the myelin decomposition product. Regeneration took place almost immediately and was first observed as a proliferation of the Schwann cells and by an unravelling of the axons into numerous fibrils. Regenerating nerve fibers were present 5 days after suture within the original endoneural tubes in the proximal segment, frequently accompanying old axis cylinders and always attached to proliferating Schwann cells. In the traumatic zone where the irregular proliferation of the endoneural mesodermal cells had changed the original nerve structure and where traumatic myelin products were present, numerous Perroncito spirals were found.

Mesodermal and ectodermal cellular proliferation, followed by the formation of numerous capillaries, took place simultaneously in the distal segment of the nerves repaired by end-to-end suture. Regenerating nerve fibers entered the suture line following the path of proliferating histiocytes in the granulation tissue during the first week after suture. They were closely attached to the proliferating cells and were accompanied by newly formed fine collagenous fibers. Beyond the small traumatic zone in the distal segment, the regenerating nerve fibers were seen in close contact with the cellular endoneurium and the Schwann cells in the outer zone of the endoneural tubes which were filled with decomposed myelin and the fat globules characteristic of Wallerian degeneration. From one axon a large number of fine fibrils might sprout and fan out in all directions into the suture line along the scaffolding laid down by the proliferating mesodermal cells.

The trauma also caused a reactive epineural proliferation which had the characteristics of a symptomatic inflammation. This proliferation took place on the surface of the proximal and distal segments as a continuation of the mesodermal reaction of the suture line. The epineural reaction lost its chronic inflammatory character and decreased gradually as time went on. Some of the regenerating nerve fibers, fanning out at the suture line, followed the proliferating mesodermal elements outside the limits of the nerve into the proliferating epineurium and perineurium. These deviating epineural nerve fibers have been observed over the distal segment and also over the proximal segment where they took a retrograde course and often penetrated deep into

Fig. 5. Autogenous graft 120 days after transplantation showing an isomorphous structure and neurotization similar to that of a regenerating peripheral nerve. The old endoneurium is preserved and directs the band and nerve fiber proliferation. Remaining myelin decomposition products show the arrangement of the original neurilemma tubes characteristic of a degenerating nerve. The borderline between perineurium and nerve fascicle is preserved. (Bodian-fuchsin stain, ×90.)

the perimysium of the surrounding muscles. These fibers were lost for ultimate function.

The formation of thick and well developed axis cylinders was rarely observed in the distal segment 30 days after the suture, in contrast to the large amount of fine nerve fibers present, but was well under way after 45 and 60 days. The formation of myelin sheaths was practically absent after 30 days, just beginning after 45 days, and well recognized 60 days after suture. The amount of myelin decomposition products was large after 30 and 45 days and had only slightly decreased after 60 days (Fig. 4).

Even in the cat it was an exception that an autogenous graft healed like a nerve sectioned at two sites and repaired by end-to-end sutures. The ectodermal elements of the graft underwent a necrobiotic process and only the mesodermal elements remained alive. The myelin degeneration process was different from Wallerian degeneration. It also seemed that the Schwann cells became necrotic, possibly as a result of ischemia. The mesodermal endoneural cells, however, usually survived and were an important factor in the preservation of the original structure of the graft. They proliferated almost immediately after implantation of the graft and thus paved the way for the regenerating nerve fibers which,

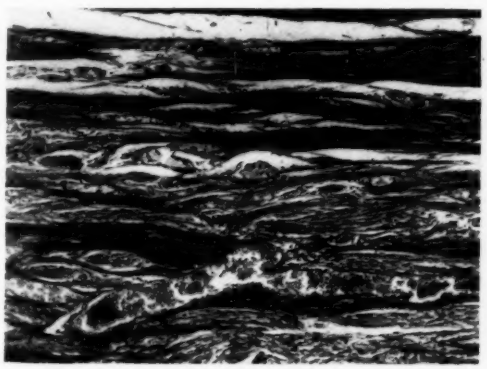

Fig. 6. Homogenous graft 90 days after transplantation showing an entirely heteromorphous structure and neurotization. The borderline between the perineurium and nerve fascicle has been destroyed and bundles of band fibers and regenerating nerve fibers pass between dense strands of proliferating collagenous fibers into the perineurium. (Bodian-fuchsin stain, ×95.)

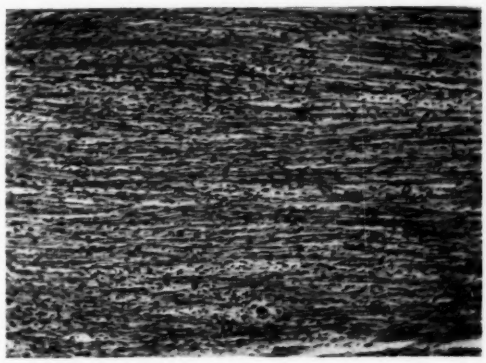

Fig. 7. Homogenous graft 90 days after transplantation showing a mixed isomorphous and heteromorphous structure and neurotization. There is a marked proliferation of mesodermal and Schwann cells and thick collagenous fibers run parallel to the regenerating nerve fibers. (Bodian-fuchsin stain, ×95.)

accompanied by outgrowing Schwann cells, followed the old endoneural tubes (Fig. 5). Even in the most favorable such an isomorphous[1] structure was never seen throughout the graft; there was always some irregularity or excess proliferation of the old endoneurium which caused some branching off and confusion of the regenerating nerve fibers, especially in the periphery of the graft. The borderline between perineurium and nerve fascicles remained intact. Some regenerating nerve fibers from the suture lines which penetrated the proliferative epineurium of the graft and proximal and distal segments could be traced for short distances but usually got lost. Once the regenerating nerve fibers had reached the distal suture line they found their way satisfactorily through the mesodermal granulation tissue and the mesodermal fibers of the suture line into the distal nerve segment. Six days after implantation of an autogenous graft, a purely mesodermal junction was established by the endoneural mesodermal elements and the perineurium of the graft and proximal and distal segments. Regenerating nerve fibers

[1]The term "isomorphous" is used to describe the structure of a graft in which the original neurilemma tubes are preserved and form a straight downward and parallel pathway for the regenerating band and nerve fibers. It has a similar aspect to that of a regenerating peripheral nerve which has undergone Wallerian degeneration. We use the term "heteromorphous" structure to characterize the disappearance of the original nerve structure within a graft and its replacement by a network of mesodermal fibers which lead the regenerating band and nerve fibers in an irregular and deviating course.

were present at the proximal suture line while the ectodermal elements of the graft were in a state of complete degeneration. Fourteen days after implantation of the graft, the regenerating nerve fibers had penetrated the graft following the path of the old endoneural tubes. The grafts were well neurotized throughout their entire length on the 45th day; nerve fibers had already penetrated the distal nerve segment for several centimeters. Beginning formation of axis cylinders could also be observed in the grafts only, but no myelin sheaths were present. On the 60th day axis cylinders were seen in the distal nerve segment and the formation of myelin sheaths began in the graft.

The neurotization of an homogenous graft was a different process. The ectodermal tissue and most of the mesodermal elements underwent total necrosis. Some mesodermal elements survived transplantation in some isolated superficial areas of the graft where the blood flow was soon re-established. The myelin underwent a necrobiotic process of dissolution without forming fatty end products, and true necrotic material was finally organized in later stages by mesodermal macrophages and other histiocytic elements arising from the surrounding tissues. There was an almost complete destruction of the original endoneural structure. This destruction became more obvious where sprouting histiocytes and fibroblast entered the necrotic areas. The mesodermal cellular proliferation preceded the appearance of the Schwann cells and regenerating nerve fibers. Large bundles of collagenous fibers grew into the dense meshwork of proliferating endoneural cells and fibers and contributed a great deal to the structural confusion which characterized most of the homogenous grafts. The original nerve structure was thus replaced by a neuromatous type of tissue in which the regenerating nerve fibers did not follow a parallel course. The confused course followed by the regenerating nerve fibers gave rise to a heteromorphous neurotization, in comparision to the isomorphous neurotization which took place in autogenous grafts. In many areas the mesodermal proliferation led also to an obliteration of the original perineural limits, so that the whole mass of the nerve fascicles with their perineurium formed a sort of neuromatous mass (Fig. 6). A large amount of regenerating nerve fibers took their course between the proliferating strands of the epineural collagenous fibers. In some instances the epineurium contained more regenerating nerve fibers than the original nerve fascicles of the graft. These epineural nerve fibers were in contact with numerous Schwann cells and in due time formed myelinated axons. Myelin decomposition products remained present for a long time within the graft and also contributed to its heteromorphous structure. Of course, the isolated areas of the graft in which the endoneural structure was preserved showed an isomorphous organization and neurotization (Fig. 7).

The suture lines were similar in structure to those in autogenous grafts. The mesodermal junction established at the suture lines was formed by proliferating elements from the proximal and distal nerve segments and not from the graft. Ten days after transplantation, the graft was completely necrotic but some mesodermal reaction and proliferation had already taken place. After 21 days there was a marked proliferation of the perineurium and epineurium, and neurotization had taken place in the proximal end of the graft. In 45 day old grafts the regenerating nerve fibers had grown through the entire graft, the distal suture line and had begun to advance in the distal nerve segment. The neurotization of the grafts was usually very good 75 days after transplantation, although necrotic products were still present in large amounts. The neurotization of homogenous grafts was irregular, often incomplete and delayed, depending upon the amount of necrosis which had taken place, the vascularization, and the rate of absorption of the necrotic products. Most of them showed, however, a satisfactory neurotization 75 days after transplantation of the graft.

Alcohol-fixed homogenous grafts showed the same picture as the necrotic portion of fresh homogenous grafts. Their neurotization was much poorer within the fascicles which had to be organized by ingrowing mesodermal

elements and capillaries. Large necrotic areas remained unorganized for a considerable length of time and most of the neurotization was epineural. Although a great number of regenerating nerve fibers were lost within the graft, the nerve fibers which grew along the epineurium, in spite of all the obstacles, led to a satisfactory regeneration of the distal segment. In these cases, however, the recovery of function was greatly impaired.

CLINICAL OBSERVATIONS

After severance of the sciatic nerve in the thigh the most evident symptoms were the paralysis of the leg, foot, and toes and the loss of sensation in the area supplied by the sensory fibers of the tibial, peroneal, and sural nerves. The animals were examined at various intervals after nerve repair, and observations upon return of function were made in the following manner:

1. Motor signs—presence and degree of heel and toe drop, presence and production of voluntary movements in the foot and toes.
2. Muscular contractures—presence and degree of limitation of motion of muscle groups as compared to the healthy side.
3. Muscle atrophy—presence and degree of atrophy as compared to healthy side.
4. Sensory signs—response to pin prick and to pinching the foot and toe pads.
5. Trophic signs—presence of thickening and dryness of the skin of the foot and toe pads, presence and degree of trophic heel ulcers.
6. Reflex signs—presence of fanning reflex of the toes, of step, and ankle reflexes.
7. Response to direct electrical stimulation of the exposed sciatic nerve.

In order to evaluate properly the various signs of recovery, it was necessary to have an exact knowledge of the anatomy of the posterior extremity of the cat which in many ways differs from that of the human. For that purpose careful dissections of the extremity were performed upon dead and anesthetized animals, in which the various branches of the sciatic nerve could be stimulated electrically, while other branches were cut, and their selective motor responses studied. In several animals the various muscular branches and the distal tendons of the leg and foot muscles were isolated and cut, and the various responses to electrical stimulation observed, thus giving a clear picture of the selective action of each muscle and confirming the anatomical nerve supply of each muscle. The strength of current used for stimulating these nerves (0.1 volt) was never sufficient to produce a local contraction when applied to the muscle itself and great care was taken not to touch adjacent tissue with the electrodes when stimulating isolated nerves.

The sensory components of the sciatic nerve in cats are formed by small branches which the tibial nerve gives off in its course, by the entire distal portion of the superficial peroneal nerve and by the entire sural nerve, which branches off the sciatic nerve about 1 centimeter above its division in the lower portion of the thigh. The tibial nerve supplies most of the muscles which produce plantar flexion of the foot and the toes. Electrical stimulation of the sciatic nerve above its division produced plantar and dorsiflexion of the foot and toes, inversion and eversion of the foot, abduction of the heel, abduction and adduction of the toes, and protrusion of the claws. Stimulation of the common peroneal nerve produced dorsiflexion of the foot and toes and abduction of the toes. When the deep peroneal nerve was stimulated at the ankle, dorsiflexion of the proximal phalanges and abduction of the toes were observed, producing the picture of fanning. Stimulation of the tibial nerve in the popliteal fossa gave rise to plantar flexion of the foot and toes, abduction of the heel, adduction of the toes, and protrusion of the claws. When it was stimulated at the ankle, plantar flexion of phalanges and adduction of the toes were observed. Important for our study is the fact that the peroneus tertius, which is a long and well developed leg muscle, is supplied by a proximal branch of the superficial peroneal nerve, and that abduction of the toes is performed by muscles which are supplied by the deep peroneal nerve.

An important factor in evaluating the period at which the signs of functional recovery are first observed is the length of the course the regenerating nerve fibers have to travel until they reach their end organs in

the muscle or skin. Thus in an average cat, the proximal site of repair lies 50 millimeters above the division of the sciatic nerve. The sural nerve leaves the sciatic nerve 40 millimeters below the site of suture. The length of nerve between the proximal site of repair and the entrance into the lateral head of the gastrocnemius is 80 millimeters, the medial head of the gastrocnemius, 75 millimeters, the anterior tibial, 120 millimeters, the extensor digitorum longus, 130 millimeters, and the flexor digitorum longus, 105 millimeters. The distance to the ankle along the tibial nerve measures 185 millimeters and along the deep peroneal nerve 190 millimeters. The length of the deep peroneal nerve and its divisions from the transverse ligament of the ankle to the proximal border of the foot pad is 60 millimeters, and of the tibial nerve and its divisions to the base of the metatarsal bones, 60 millimeters.

MOTOR SIGNS OF RECOVERY

a. Gait and stance. The majority of the experimental animals were cats which normally walk and stand on the plantar surface of their toes only. It is only in the sitting position that the entire foot touches the ground. Paralysis of the muscles below the knee produced a gait characterized by a dragging forward of that extremity so that the toes were passively plantar flexed by friction on the floor. The animal thus bore its weight on the dorsum of the toes instead of the plantar surface. This is described hereafter as "toe drop." In walking it appeared that the cat was able to elevate the heel from the floor even though the gastrocnemius muscle group was completely paralyzed. This lifting of the foot is performed by muscles above the knee which raise the knee and the leg. When the animal stood still and bore its weight on the posterior foot pads, it was then apparent that it could not elevate the paralyzed heel from the floor. This is described hereafter as "heel drop."

The disappearance of the heel drop sign was not a sign of early recovery of gastrocnemius function, as one could demonstrate movements in the gastrocnemius muscle group by other means sometime before the cat had enough power to elevate the heel off the floor when standing. For a similar reason, the disappearance of the toe drop could not be considered as a sign of early recovery of the anterior tibial muscle group. Furthermore, in some instances the cats developed contractures of the plantar flexors of the toes and of the dorsal flexors of the foot so that they never regained the ability to walk and stand on the toe pads even though they had good function in the dorsal and plantar flexors of the foot and toes.

In the animals which recovered without complications, normal gait and normal stance were regained. Following end-to-end sutures heel drop started to disappear 45 days after nerve repair and a nearly normal standing position was regained after 60 days. Toe drop remained present after 60 days and began to disappear 90 days after nerve repair. In autogenous grafts heel drop started to recover after 60 days; it had disappeared in 66 per cent of the animals after 90 days and was practically gone 150 days after implantation of the graft. Toe drop was present in all cases after 75 days, and began to disappear in 17 per cent of the animals after 90 days. However, it was still present in 50 per cent of the animals 150 days after implantation of the graft. In homogenous grafts heel drop was present in all animals after 75 days; it began to disappear after 120 days, and after 150 days all animals showed some recovery. Toe drop was present in all animals 150 days after implantation of the graft.

b. Motion. Motion was tested by provoking contractions of the leg and foot muscles by painful stimuli, such as tapping the site of nerve repair, compressing the area of emergence of the roots of the sciatic nerve from the spinal column, pressing upon the bones of the leg, foot, and toes and by pinching the skin of the leg and foot. To ascertain thus the presence of motion it was necessary to fix the knee or the ankle joint at a right angle in order to avoid the occurrence of supplementary motion resulting from movements of the thigh or hip. By these methods, recovery of motor function was detected earlier than was the appearance of normal gait or stance, or the recovery from heel drop. The earliest

movement elicited was plantar flexion of the foot, followed by plantar flexion of the toes and dorsiflexion of the foot. Dorsiflexion of the toes and fanning of the toes appeared much later.

Plantar flexion of the foot could be produced in all end-to-end suture experiments after 60 days. In autogenous grafts this movement appeared between the 60th and the 82nd day, averaging 70 days after implantation of the graft. In the same graft the average day of appearance of plantar flexion of the toes was the 71st, and of dorsiflexion of the foot, the 79th day. Dorsiflexion of the toes could be provoked only in 33 per cent of the animals at the 90th day and in 60 per cent on the 120th day and fanning of the 5th toe alone in 17 per cent of the animals on the 76th day and 80 per cent on the 120th day. In homogenous grafts occasionally some isolated motion could be produced 60 days after implantation, but even after 90 and 120 days, very few voluntary movements could be elicited.

MUSCULAR CONTRACTURES

In order to study the presence and degree of muscle contracture, the normal and the operated upon extremities were examined at the same time and in the same fixed position. Muscular contractures manifested themselves by a limitation in the range of motion in the involved joint. Usually the contractures were mild so that with a little tension the muscle groups could be stretched to their normal length. In other instances the contractures were so obvious and so rigid that tension produced pain and did not increase the range of motion.

No significant contractures were found in the hamstring muscles and the knee could be extended in all cases. Neither were significant contractures found in the gastrocnemius muscle group; the feet could always be easily flexed against the anterior surface of the leg.

In testing the contractures of the anterior tibial muscle, the knee was passively extended and the ankle would assume a position of 180 degrees' extension. A slight contracture of the anterior tibial muscle was occasionally present, usually less than 30 degrees, so that the ankle could be extended to about 150 degrees. The extensor digitorum longus was examined with the knee flexed at a right angle and, when normal, the ankle could be extended to 180 degrees. Contracture of this muscle group was the most common. It was usually associated with contracture of the dorsiflexors of the foot, but was much more involved. In some cases it was present alone. The contractures of this muscle varied between 15 and 90 degrees. In the case of 90 degree contractures, the ankle could not be extended further than a right angle with the leg.

The flexor digitorum longus was examined when the ankle was maintained at a right angle and the knee in an acute degree of flexion. The toes could then normally be dorsiflexed 90 degrees and plantar flexed 90 degrees from the horizontal. When the flexors of the toes were contracted the dorsiflexion was limited and, in extreme cases, the toes could not be moved from extreme plantar flexion, which would represent a 180 degree contracture. Contractures of the flexor digitorum longus were less common than those involving the dorsiflexors of the toes and foot, but when this muscle group was involved the contractures were usually more severe, and 90 and 180 degree contractures were not uncommon.

Only the obvious contractures have been taken into consideration in the majority of the animals. None was observed in 30 animals with end-to-end sutures kept alive for various periods of time up to 90 days. Among a group of 39 animals with autogenous grafts, two severe contractures of the extensor digitorum longus and one of the flexor digitorum longus were observed. In another group of 20 animals with autogenous grafts, especially studied from a clinical standpoint, the anterior tibial muscle group showed mild contractures in 6 animals rating from 15 to 30 degrees; the extensor digitorum longus showed contractures in 8 cases; 6 of them associated with the previous group and the extent of the contractures varied from 15 to 70 degrees. The flexor digitorum longus showed contractures in 5 cases; 2 of 15 degrees, 1 of 30 degrees, and 2 of 90 degrees. Thus contrac-

tures were noticed to some degree in 55 per cent of this group of autogenous grafts. They were first noticed after 21 days in 1 animal; 30 days in 3 animals; 45 days in 2 animals; 60 days in 2 animals; and 70 days after implantation of the graft in 2 animals. These cats were allowed to live 90 or 120 days, and the extent of the contractures increased in severity. In a group of 50 homogenous graft animals, severe contractures were noticed in 6 cases and involved especially the extensor digitorum longus muscle group.

Obviously, most of the contractures occurred during the stage of complete denervation and were a result of the bad position assumed by the paralyzed extremity, described here as toe and heel drop. The former produced a shortening of the plantar flexors of the toes and the latter a shortening of the dorsiflexors of the foot and toes. Motor recovery and response to direct electrical stimuli were observed in the contracted muscles as well as in the other normal ones.

MUSCLE ATROPHY

Atrophy took place in all of the muscles temporarily denervated. The loss of muscle weight was directly proportional to the period of denervation. It reached its peak between the 15th and 45th day, and as reinnervation took place, the paralyzed muscles slowly and gradually regained weight.

During the examination it was always obvious that the gastrocnemius muscle group had lost a large amount of its volume and often could be palpated as a small stringlike organ. This was especially true and noticeable in animals with homogenous grafts. At autopsy the gastrocnemius and plantaris muscles were removed in one group and weighed; the affected side being compared to the healthy side. In a certain number of animals the anterior tibial and the extensor digitorum longus muscles were weighed and compared. The range of atrophy varied and remained wide even within the groups of animals which were allowed to recover the same length of time. The loss in weight in the gastrocnemius muscle group was usually larger than in the anterior tibial group. The amount of muscle atrophy was obviously higher in all of the animals in which the distal suture line of the graft had been resected and resutured because this procedure prolonged the time of denervation. For this reason this group cannot be compared to animals in which the distal suture line was not resected.

Thirty days after end-to-end sutures, the loss of weight of the gastrocnemius muscle varied between 53 and 64 per cent. In 90 day old autogenous graft experiments the loss of weight of the gastrocnemius was between 18 and 39 per cent, the average being 30.4 per cent and in the anterior tibial muscle it varied between 19 and 46 per cent with an average loss of 26.4 per cent.

Comparing animals with autogenous and homogenous grafts which had undergone the same kind of treatment for the same period of time, the gastrocnemius lost an average of 59 per cent of its weight within 90 days in autogenous and 72 per cent in homogenous grafts. One hundred and fifty days after implantation of the grafts the average loss of weight for the same muscle group was 45 per cent in autogenous and 54 per cent in homogenous grafts.

It is of interest to note that the specific gravity of the atrophied muscles was constantly slightly less than that of normal muscles. Comparing the diseased to the healthy muscles in autogenous grafts, the average specific gravity of the gastrocnemius muscle group was 1.0605 to 1.0675 and of the anterior tibial group 1.0611 to 1.c698.

Another interesting fact is that in animals which were allowed to recover 21 to 33 months after nerve repair, the formerly paralyzed and atrophied muscle groups showed a tendency to become hypertrophic. Thus, in a group of 5 animals with autogenous grafts, 5 animals with homogenous grafts, and 1 end-to-end suture animal, hypertrophied muscles were found in 8 instances. When compared to the same muscle groups of the healthy side they showed an increase in weight up to 15 per cent. In some cases only the anterior tibial group, or the gastrocnemius group, showed some hypertrophy while the opposite group was still slightly atrophied. In 5 of the 11 animals hypertrophy was present in both muscle groups. Three animals still showed

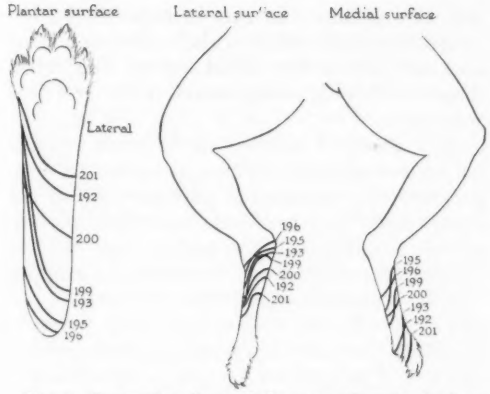

Fig. 8. Composite chart of the area of analgesia in a group of cats 90 days after transplantation of an autogenous graft in the left sciatic nerve. The numbers indicate the identification number of the animal.

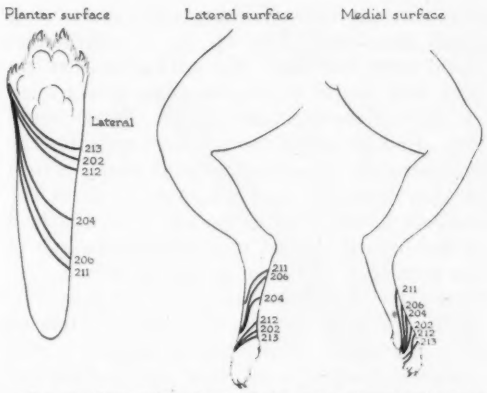

Fig. 9. Composite chart of the area of analgesia in a group of cats 120 days after transplantation of an autogenous graft in the left sciatic nerve. The numbers indicate the identification number of the animal.

marked atrophy from 18.3 to 49.5 per cent in the gastrocnemius group and from 4.2 to 6.7 per cent in the anterior tibial group, 23 to 25 months after nerve repair. The cases in which this severe atrophy was present were also characterized by marked muscle contractures and two of the three animals had large heel ulcers which did not show any tendency to heal. The animals with the hypertrophic muscles had no, or minimal, contractures and no trophic ulcers.

SIGNS OF SENSORY RECOVERY

The only sensation that could be tested was that of pain, as evidenced by response to pin prick, and pressure or deep pain.

a. Response to pin prick. The pin pricks were started in the anticipated anesthetic area and carried upward on the extremity until the cat gave some recognition of pain by crying or withdrawing the extremity. In this manner the anesthetic area could be demarcated. Pain sensation was tested 30, 45, 60, and 75 days after nerve repair. Marked differences in the area of analgesia were present in the animals tested during the same postoperative periods. Since the site of nerve repair was approximately the same in all animals, these differences were probably due to anatomical variations in the sensory supply and the degree of overlap to those areas. Thus in some animals, 30 days after end-to-end suture, the analgesic area on the medial surface of the foot extended from the heel downward, while in the other animals it was localized to the phalanges of the 2nd toe. In all animals, however, the entire lateral and plantar surfaces of the foot were completely analgesic. For this reason the return of sensation on the medial and dorsal surfaces of the foot could not be considered as a criterion for recovery.

The area of isolated sensory supply to pain of the sciatic nerve in the cat consists of the lateral and plantar surfaces of the foot and also includes the lower third of the lateral surface of the leg. In the other areas an overlap of sensory function by adjacent uninjured nerves, such as the long saphenous, must be considered. The critical areas of sensory recovery were thus limited to the external and the plantar surfaces of the foot and to the toes.

In end-to-end sutures no response to pin prick could be obtained below the heel after 30 and 45 days. Sixty days after suture, pain sensation could be found around the heel in the area covering approximately one-fourth of the plantar and lateral surfaces of the foot.

In autogenous and homogenous grafts no critical return of pain sensation was found after 75 days. Sixty days after secondary resection and resuture of the distal suture line of the grafts sensory recovery was occasionally

found in the case of autogenous grafts in a small area extending up to 2 centimeters distal from the heel. No critical sensory return was found in homogenous grafts even 75 days after resuture of the distal suture line. In a group of animals 90 days after the implantation of an autogenous graft, return of pain sensation was observed in all of the animals in the area extending from the heel to half of the lateral and plantar surfaces of the foot (Fig. 8). In a group of animals 120 days after the implantation of an autogenous graft, the area of sensory return extended from the middle of the plantar surface to the proximal border of the foot pad and on the lateral surface from its middle to the beginning of the proximal phalanx of the fifth toes (Fig. 9).

In long term animals complete sensory recovery was found 1 year after the implantation of autogenous or homogenous grafts, as well as after repair by end-to-end suture.

b. Response to pressure or deep pain. Compression of the toe pads produced a response observed as a withdrawal of the whole extremity. This withdrawal sign was considered as a test performed by muscles above the knee. After section and repair of the sciatic nerve, the animals did not respond to compression of the toe pads for a long period of time. It was considered that the extent of isolated loss of deep sensation of the sciatic nerve that could be tested with any degree of accuracy was restricted to the pads of the 2nd, 3rd, 4th, and 5th toes.

The earliest response to deep pain was observed on compression of the 2nd toe. It was occasionally elicited 30 days after an end-to-end suture but was present in only 50 per cent of the animals 60 days after end-to-end suture. At that time 30 per cent of the animals responded to compression of the other toes as well.

After repair by autogenous and homogenous grafts, response to compression of the 2nd toe was rarely present within the first 75 days. This isolated response, however, was present in most autogenous grafts 60 and 75 days after secondary resection and resuture of the distal suture line of the graft and a response from compression of the 3rd and 4th toes was also obtained in rare instances. In homogenous grafts even 75 days after resection and resuture of the distal suture line, withdrawal following compression of the 2nd toes was rare.

In a group of animals 90 days after repair by an autogenous graft no response to deep pressure was obtained in 28.5 per cent of the cases, while 71.5 per cent responded to compression of the 2nd toe and 43 per cent to compression of all toes. In a group of animals 120 days after an autogenous graft repair, 16 per cent did not respond to deep pressure while 84 per cent responded to compression of the 2nd toe and 66 per cent to compression of all toes.

SIGNS OF TROPHIC DISTURBANCES

The foot and the four toe pads of the cat are normally soft, moist, and very sensitive to pain. After section of the sciatic nerve they became pale, dry, thick, coarse and horny, and desquamation of the horny layers took place. These skin changes persisted a long time after repair of the sectioned nerve. They remained that way 60 days after end-to-end suture and 75 days after the implantation of grafts.

In a group of 90 autogenous graft experiments, a slight change was found in the foot pads of only 14 per cent of the animals. When recovering, they first lost their thick and horny appearance and became soft, still they remained dry. One hundred and twenty days after implantation of an autogenous graft, 50 per cent of the animals showed some recovery in the texture and the appearance of the foot and toe pads.

Another trophic change which occurred was the formation of an ulcer on the plantar surface of the heel. Normally, a cat never stands or walks on its heel and the skin of the heel is delicate. The lesion of the heel was in most cases very mild and consisted in a circular loss of hair and thickening of the underlying skin. In a small group of animals, however, an ulcer developed and produced marked inflammatory reactions. The ulcers showed a soft necrotic and bleeding base which was surrounded by a thick, circular wall. The animals developed the ulcers between the 30th

and 45th day after nerve repair. Most of them occurred after implantation of grafts, especially if the graft was homogenous.

Only one of the 30 animals developed an ulcer (3.3 per cent) after end-to-end suture; 4 of the 65 animals with autogenous grafts developed an ulcer (6.2); and 6 of the 50 animals with homogenous grafts had an ulcer (12 per cent). In some cases the ulcers healed spontaneously 45 to 60 days after their appearance. Most of them, however, persisted until the specimen was removed; in 2 cases the ulcer was still present after the 25th month. Eight animals which had no heel ulcer developed one after secondary resection and resuture of the distal suture line of the graft; 3 of these had autogenous and 5 homogenous grafts. In 2 animals the ulcer involved the bone and marked contractures developed, fixing the foot at a right angle with the leg and preventing dorsiflexion of the toes.

Some limitation of movements was present in some of the other cats which had ulcers, but it was not more prominent than in the animals which had no ulcers. The ulcers retarded clinical recovery, as they were painful and the animal avoided movement of the leg and avoided stepping on the affected foot. Large suture line neuromas were found in 3 cases which had developed ulcers, and in 5 cases the amount of adhesions around the grafts and the suture lines was large, but the microscopic sections showed good neurotization of the distal nerve segment. Response to electrical stimulation, however, showed the normal signs of recovery in all of the tested muscle groups.

The claws on the affected side were usually longer and thicker on the normal side. Sheathing of the claws was occasionally observed together with the recovery of the texture and appearance of the foot and toe pads, but these observations were not followed sufficiently well to ascertain the return to normal appearance and growth of the claws.

RETURN OF REFLEXES

The *fanning reflex* is elicited by allowing the cat to fall rapidly when it is suspended by the skin of the back of the neck. The toes of the normal side fan out but on the paralyzed side the toes remain together and no fanning occurs.

This reflex is a very late and inconstant sign of recovery, and when it is present it is usually incomplete. In a few isolated cases an abduction of the 5th toe alone has been observed while the other 3 toes did not move when the animal was dropped. The abduction of the 5th toe, however, is produced by a contraction of an isolated muscle of the leg, the peroneus tertius, which is supplied by a branch of the superficial peroneal nerve. The fanning of the other toes is produced by contractions of the short muscles of the foot and toes, supplied by distal branches of the deep peroneal nerve.

The fanning reflex of the 5th toe was observed in one case of end-to-end suture after 60 days; in 2 cases of autogenous grafts after 60 days, in one autogenous graft after 80 days, and in another one after 90 days. In a group of 13 end-to-end sutures, autogenous and homogenous graft experiments which were allowed to recover for a period of 2 to 3 years, a slight fanning reflex of all the toes was observed only once, and that occurred in an animal with a homogenous graft.

Fanning of the toes as a response to direct electrical stimulation of the nerve is also a late sign of recovery, but it has been obtained in a large number of animals in which the reflex could not be elicited. The same applies to the fanning of the toes obtained as a response to painful stimuli.

The *step reflex* is elicited by suspending the cat by the back of the neck and permitting the dorsal surface of the hind paws to rub lightly against the projecting edge of a table. On the normal side the whole lower extremity responds by a step-like movement, while the paralyzed extremity hangs limply without response. When function returns a slight dorsiflexion of the foot occurs, which is later followed by a slight plantar flexion of the foot, producing feeble step-like movements. This beginning return of the step reflex has been found only in isolated animals a long period of time after nerve repair. A normal step reflex, which also included movements of the toes, has never been observed, even in animals which were allowed to recover for 34 months.

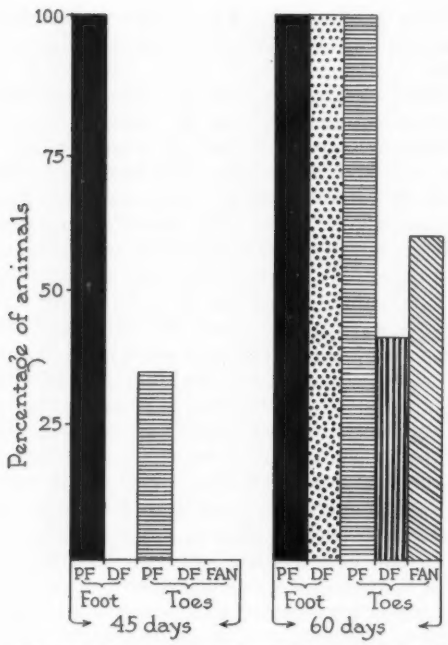

Fig. 10. Response of various muscle groups to direct electrical stimulation of the sciatic nerve 45 and 60 days after end to end suture. *PF*, plantar flexors; *DF*, dorsiflexors; *FAN*, abductors and adductors.

The *Achilles reflex* was not constantly tested as it is difficult to obtain in a normal cat. It was observed in a few animals 90 and 120 days after the implantation of an autogenous graft and it occasionally seemed to be more active than on the healthy side.

All reflexes were found to be late and inconstant signs of recovery. They could be elicited only in a very small number of animals and thus are of no great statistical value.

RESPONSE TO ELECTRICAL STIMULATION

Whenever it was necessary to expose the repaired sciatic nerve, whether it was when the specimen was removed or when the distal suture line of the graft was resected and resutured, the nerve was electrically stimulated and the responses were tabulated. Stimulation was performed with a stimulator designed by Hinsey and Geogehan which produced an alternating current of sine wave form of a frequency of 60 cycles per second and made it possible to measure the voltage necessary to produce a muscular contraction. The exposed nerve was stimulated with platinum electrodes at various levels above, on, or below the suture lines and on the grafts. The tibial and the common peroneal nerves were stimulated in the popliteal fossa and the tibial and the deep peroneal nerves at the level of the ankle. The reading of the voltameter was taken when the stimulus was strong enough to produce a definite motion as a result of small contractions of the flexor or extensor groups of the foot or toes. Thus the following motions were considered: plantar flexion of the foot, plantar flexion of the toes, dorsiflexion of the foot, dorsiflexion of the toes, fanning of the 5th toe, fanning of all toes, inversion and eversion of the foot, abduction of the heel, flexion and extension of the proximal phalanges of the toes. For critical examination the least amount of current necessary to produce plantar flexion of the foot and toes, dorsiflexion of the foot and toes and fanning of the toes was recorded. In the normal sciatic nerve the average threshold needed to produce these various movements was 0.1 volt.

a. End-to-end sutures. No response was obtained from 30 day animals. In the 45 day group 33 per cent of the animals had 40 per cent of the normal total electrical response, and 67 per cent gave 20 per cent of the normal response. This means that 100 per cent of the animals responded with plantar flexion of the foot and 33 per cent with plantar flexion of the toes. In the 60 day group 30 per cent of the animals scored 100 per cent electrical response; 40 per cent scored 80 per cent and 30 per cent scored 60 per cent of the total electrical responses. Considering the various muscle groups, 100 per cent of the animals had plantar flexion of the foot, plantar flexion of the toes and dorsiflexion of the foot, while only 40 per cent responded with dorsiflexion of the toes and 60 per cent with some fanning of one or more toes (Fig. 10).

b. Autogenous grafts. No response was obtained from electrical stimulation of the nerve or graft 45 days after implantation of the graft. In 60 day old grafts plantar flexion of the foot and plantar flexion of the toes could be obtained in 33 per cent of the animals.

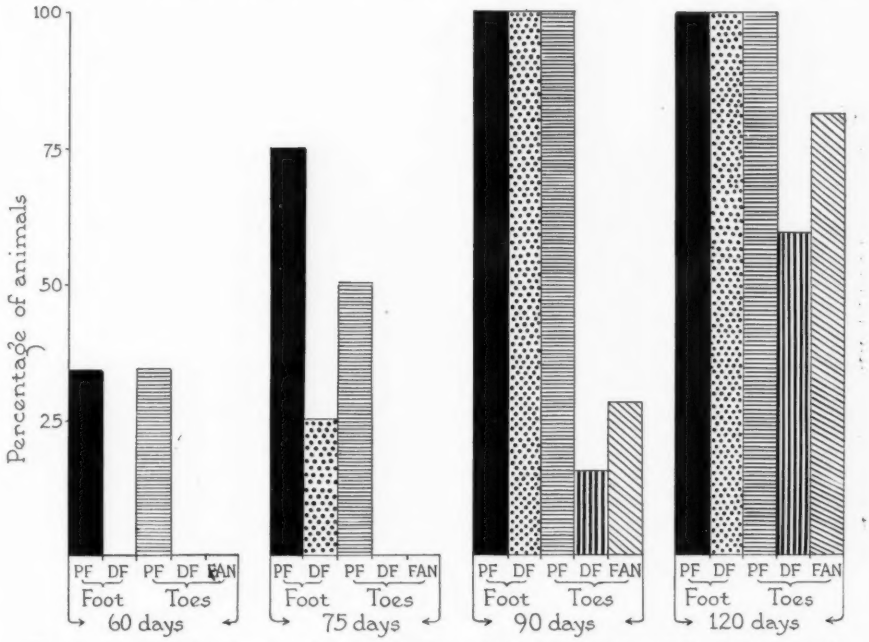

Fig. 11. Response of various muscle groups to direct electrical stimulation of the sciatic nerve 60, 75, 90, and 120 days after transplantation of an autogenous graft. *PF*, plantar flexors; *DF*, dorsiflexors; *FAN*, abductors and adductors.

In 75 day old grafts, plantar flexion of the foot was obtained in 75 per cent, plantar flexion of the toes in 50 per cent and dorsiflexion of the foot in 25 per cent of the animals. In 90 day old grafts, plantar flexion of the foot and toes and dorsiflexion of the foot was obtained in 100 per cent, dorsiflexion of the toes in 14 per cent, and fanning of the toes in 29 per cent of the animals. In 120 day old grafts plantar flexion of the foot and toes and dorsiflexion of the foot was present in 100 per cent, dorsiflexion of the toes in 60 per cent, and fanning of the toes in 80 per cent of the animals (Fig. 11).

After resection and resuture of the distal suture line of the grafts the responses were slightly changed. Forty-five days after resection, 78 per cent of the animals presented plantar flexion of the foot and dorsiflexion of the foot, 47 per cent plantar flexion of the toes, and 6 per cent fanning of the toes. Sixty days after resection 100 per cent showed plantar flexion of the foot, 90 per cent plantar flexion of the toes, 72 per cent dorsiflexion of the foot, and 9 per cent fanning of the toes. Seventy-five days after resection plantar flexion of the foot was obtained in 90 per cent, dorsiflexion of the foot in 78 per cent, plantar flexion of the toes in 66 per cent, and fanning of the toes in 22 per cent of the animals. Ninety days after resection plantar flexion of the foot and toes and dorsiflexion of the foot were obtained in 100 per cent, fanning of the toes in 43 per cent, and dorsiflexion of the toes in 14 per cent of the animals. It is interesting to note that dorsiflexion of the toes was obtained only in the 90 day group of animals after secondary resection and resuture of the distal suture line of the graft.

c. Homogenous grafts. No response to electrical stimulation could be obtained 45 and 60 days after implantation of the graft, and after 75 days 25 per cent of the animals responded with plantar flexion of the foot.

Forty-five days after resection and resuture of the distal suture line of the graft 56 per cent of the animals showed plantar flexion of the

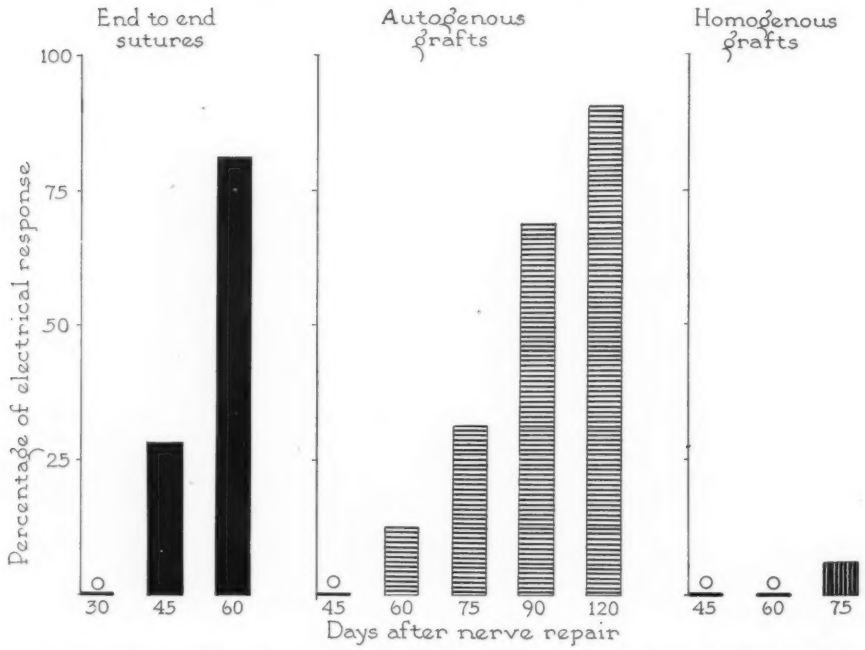

Fig. 12. Average score of total muscular response to direct electrical stimulation of the sciatic nerve repaired by end-to-end suture or by transplantation of an autogenous or homogenous graft after various periods of time.

foot, 37 per cent plantar flexion of the toes, 28 per cent dorsiflexion of the foot, and 9 per cent dorsiflexion of the toes. Sixty days after resection plantar flexion of the foot was obtained in 100 per cent, plantar flexion of the toes in 85 per cent, dorsiflexion of the foot in 56 per cent, dorsiflexion of the toes in 35 per cent, and fanning of the toes in 21 per cent of the animals. For some unknown reason, the group of animals tested 75 days after resection does not fit in the pattern of the usual responses to electrical stimulation. Plantar flexion of the foot was shown by 76 per cent, plantar flexion of the toes by 50 per cent, dorsiflexion of the foot by 40 per cent, dorsiflexion of the toes by 60 per cent, and fanning of the toes by 31 per cent of the animals.

The nerves repaired by end-to-end suture showed earlier and better responses to electrical stimulation than did those in which grafts were used. Electrical stimulation was also seen earlier in autogenous than homogenous grafts (Fig. 12). After resection and resuture of the distal suture line of the graft, the difference between response in both kinds of grafts was much less evident, although it remained slightly better in the autogenous grafts (Fig. 13).

Plantar flexion of the foot was the first response to be observed and it was closely followed by plantar flexion of the toes and dorsiflexion of the foot. Dorsiflexion of the toes and fanning of the toes were late responses. The amount of current needed to produce the responses varied between 0.01 and 0.9 volts. The more the nerve regeneration had progressed, the less current was necessary to get a response. A constant observation was that less current was needed when the suture lines were stimulated, and slightly more when the proximal and distal nerve segments were stimulated. Response to stimulation of the nerves at the ankle was obtained 60 days after end-to-end suture and 90 days after resected autogenous grafts. In animals with 120 day autogenous grafts stimulation of the tibial

nerve at the ankle produced a plantar flexion of the proximal phalanges of the toes in 100 per cent of the animals, and stimulation of the deep peroneal nerve a dorsiflexion of the proximal phalanges in 80 per cent and a fanning of all toes in 40 per cent of the animals.

B. Gunshot Experiments

The aim of the study upon experimental gunshot injuries was to produce a wound with tissue destruction and severance of the sciatic nerve the severity of which could be compared to the usual wounds of modern warfare.

The experimental methods and technique have been described in another paper. In brief, however, repair of the nerve was effected by an end-to-end suture or by the implantation of a homogenous graft.

MICROSCOPIC STUDY

When a cat's nerve is struck by a bullet severely enough only to cause a contusion and not an interruption of nerve continuity, the myelin sheaths break down in a similar manner, but to a greater degree, than is seen following sharp severance of a nerve. There is a molecular decomposition of the myelin with a localized edema, a process best called necrobiotic (Fig. 14), and entirely different from a secondary or Wallerian degeneration (Fig. 15). This necrobiosis occurs under conditions which have one factor in common; the damage to the myelin sheaths in combination with an apparent damage to the Schwann cells, with survival of the mesodermal endoneural elements. The damage to the Schwann cells seems to concern chiefly their proliferating decomposition activities. They are not destroyed in milder traumatic damage where the axis cylinders are seen to survive the demyelinization. They enter into action in later nerve fiber regeneration and remyelinization but fail in digesting the myelin.

Stimulation of the mesodermal cells, preceding nerve fiber regeneration by the nonfatty myelin decomposition products, is very clearly seen, and leads, wherever the traumatic lesion has reached a certain severity, to a confusion of the original endoneural structure and by necessity to a bewildering and irregular overproduction of regenerating nerve fibers.

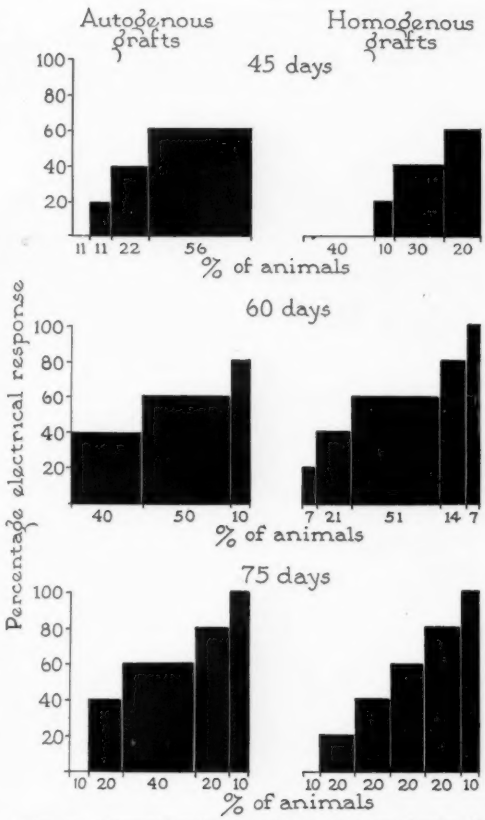

Fig. 13. Comparison between the percentage of animals and the percentage of muscular response to direct electrical stimulation of the sciatic nerve repaired by transplantation of autogenous or homogenous grafts 45, 70, and 75 days after secondary resection and resuture of the distal suture line of the grafts.

A heteromorphous nerve structure results. At a period when the neurotization is already well advanced, the myelin-detritus can still be seen between the endoneural tubes and fibers (Fig. 16). Mesodermal macrophages play the greatest part in its elimination.

Degrees of structural damage in such contused nerves may be found. The nerve with the slightest damage may show very little axis cylinder degeneration and for this reason only a relatively short transient disturbance of function; whereas in severe contusion, even without any visible macroscopic nerve lesion, a complete Wallerian degeneration of some or

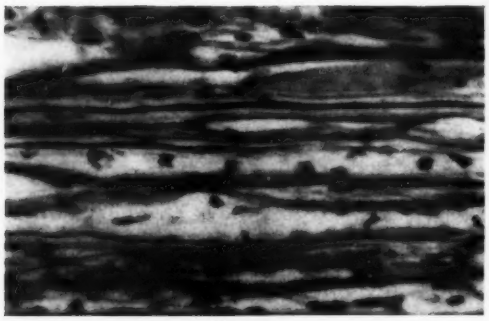

Fig. 14.

Fig. 15.

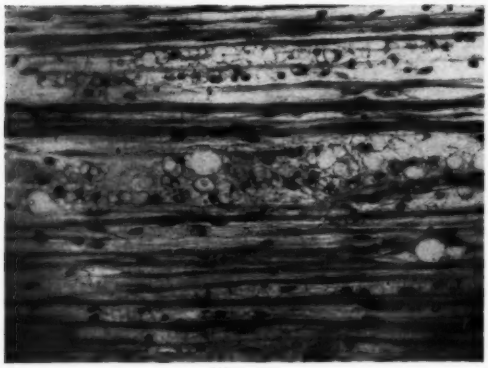

Fig. 16.

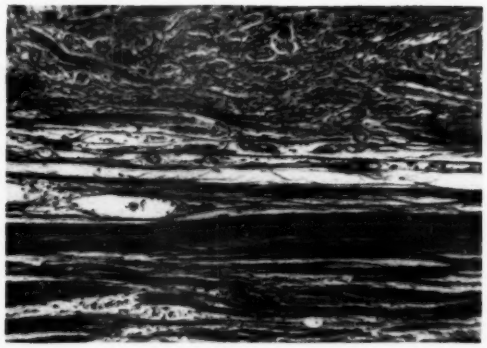

Fig. 17.

Fig. 14. Contusion of the sciatic nerve 6 days after a gunshot injury. This shows the predominantly destructive reaction of the axis cylinders within the proximal nerve segment. Some of the axis cylinders are swollen and show signs of disintegration. A relatively well preserved axis cylinder is surrounded by a swollen and partly vacuolated sheath; in other portions the myelin sheaths are partly or completely destroyed. Large amounts of detritus and edema are present mostly between the endoneural sheaths, and histiocytic elements are scattered within them. There is a general cellular proliferation of the endoneural cells; a beginning proliferation of Schwann cells, and a regenerating nerve fiber is clearly visible in the center of the picture. (Bodian-fuchsin stain, ×450.)

Fig. 15. Contusion of the sciatic nerve 6 days after a gunshot injury. It shows the distal nerve segment of the same specimen as in Figure 14, with the typical aspect of secondary degeneration. Remainders of broken down axis cylinders, degenerated myelin sheaths with myelin globules, vacuoles, and a beginning cellular reaction are present. (Bodian-fuchsin stain, ×450.)

Fig. 16. Contusion of the sciatic nerve 45 days after a gunshot injury. The distal nerve segment shows a secondary degeneration and some traumatic myelin destruction. Neutral fats lying mostly within gitter cells are accumulated near capillaries. Endoneural proliferation and nerve fiber regeneration are pronounced. (Weil stain, ×450.)

Fig. 17. Contusion of the sciatic nerve 60 days after a gunshot injury showing a severely traumatized nerve in full regeneration with a heteromorphous structure and type of neurotization. Large amounts of detritus are still present. The upper half of the photomicrograph shows the neuromatous aspect of the epineurium. In this case the bullet had traumatized the epineurium and had produced a gap in the perineurium through which numerous regenerating nerve fibers entered the epineurium. The proliferation of mesodermal cells in the epineurium was accompanied by a diffuse nerve fiber regeneration which also followed the granulation tissue of the epineurium into the adjacent muscle. The course of these regenerating nerve fibers is very irregular and just as many are seen in cross as in longitudinal sections. (Bodian-fuchsin stain, ×175.)

all nerve branches in combination with the heteromorphous type of endoneural proliferation and neurotization will be accompanied by a clinical picture similar to that produced by section of a nerve. These observations explain why some nerve contusions are followed by hardly any, or only limited, interruption of motor and sensory function; where-

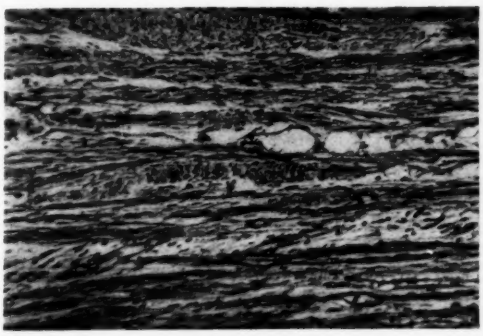

Fig. 18. Proximal segment of the sciatic nerve 30 days after end-to-end suture in a gunshot injury, showing the heteromorphous structure and neurotization in the traumatic zone. Myelin decomposition products are still present. Diffuse proliferation of the ectodermal and mesodermal endoneural elements creates a confusing course for the regenerating nerve fibers. A marked Perroncito spiral formation is present. (Bodian-fuchsin stain, ×165.)

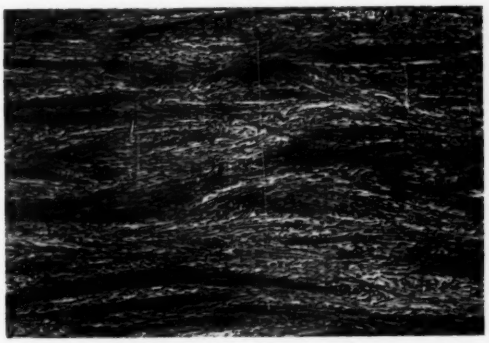

Fig. 19. Homogenous graft 90 days after transplantation into the sciatic nerve following a gunshot injury. Structure and neurotization are typically heteromorphous. Dense strands of proliferating collagenous fibers are present within the entire course of the graft. No differences were encountered in the structure of the homogenous grafts following gunshot injuries of sharp sections. (Bodian-fuchsin stain, ×190.)

as in other cases contusion leads to complete paralysis and often only imperfect return of function.

Nerve contusion may interrupt the continuity of the perineurium of nerve fascicles. This leads to a herniation of regenerating nerve fibers into the epineurium and formation of traumatic neuromas. Here again the primary endoneural fibroblastic proliferation through the perineural gap results in the sprouting of regenerating nerve fibers into the epineurium (Fig. 17). These fibers are, of course, lost for the neurotization of the degenerating part of the nerve distal to the injury.

The cat's sciatic nerve severed by a bullet differs greatly in its histological aspects from a sharply sectioned nerve. The traumatic destruction described is much more severe and extends centralward in the proximal segment not just a few millimeters, but very frequently several centimeters. This same effect may be seen reaching just as far distally in the distal segment of the damaged nerve. The effect on regeneration manifests itself in the heteromorphous type of organization and neurotization of the whole traumatized area (Fig. 18). This change is accompanied at the suture line by a greater epineural proliferation and with this there was noted an increase in the number of deviating nerve fibers fanning out from the proximal segment. This strong mesodermal reaction again seemed to be in direct proportion to the number of deviating nerve fibers.

The effect of this confusion and blockage of nerve fibers near and at the suture line of the gunshot end-to-end repair experiments is somewhat difficult to estimate in a quantitative manner, but a study of the distal nerve segments can be roughly tabulated for the sake of comparison. Microscopic examination of nerves sutured end-to-end after sharp section showed regenerated nerve fibers in the distal segment after 30 days (plus 2) in all cases; while this was increased (plus 3) after 45 and 60 days. In the gunshot specimens the regenerated nerve fibers were just beginning to be present at the end of 30 days (plus 1), while they had further progressed at the end of 45 days (plus 2) and were quite satisfactory (plus 3) at the end of 60 days. In the sharp section series the formation of thick, well developed axis cylinders, in contrast to numerous fine regenerated nerve fibers, growing in the proliferative endoneurium of the distal segment was found to be insignificant after 30 days and well under way after 45 and 60 days. The formation of myelin sheaths was likewise practically absent after 30 days, just beginning after 45 days, and well established after 60 days. On the other hand it was found that in the gunshot specimens there was just a be-

ginning of myelin sheath formation and axis cylinder formation at 45 days. This had progressed only to the status of "satisfactory" at the end of 60 days in most instances, and only rarely was considered well established by this time. Myelin decomposition products were found after 30 and 45 days (plus 3) in all cases of the sharp section series but were definitely less (plus 2) by the end of 60 days. The gunshot specimens showed a persistence of these decomposition products (plus 3) even up to 60 days. In all cases a moderate to severe amount of spongy fibrous proliferation of epineurium with marked hyperemia and some lymphocytic infiltrations was found over the central segment, and this was much more intense over the distal segment. There was also a moderately dense fibrous proliferation of the perineurium with increased vascularization and quite a few lymphocytic foci over both segments. It is true that a similar pattern was found in the sharp section series, but this was quite minimal in comparison.

There were no notable differences between the homogenous grafts of the sharp section series and those of the gunshot series in so far as the histological picture is concerned except for an occasional instance of the reaction to trauma above mentioned (Fig. 19). The reason for this lies in the fact that a graft was used in the gunshot series after large amounts of traumatized nerve had been resected, many times amounting to 3 or 3.5 centimeters. In such instances the graft then was sutured to fairly normal nerve which did not show the confusional pattern of the gunshot trauma.

MOTOR SIGNS OF RECOVERY

In the animals with end-to-end sutures no changes in the paralyzed extremity were noted at the end of 30 days; that is, they dragged the foot when walking, the ankle was flail-like, and the toes were dropped so that the dorsum presented toward the floor. After 45 days, 8 out of 18 animals showed improvement by walking with less heel drop, while after 60 days 19 out of 22 animals were improved. Of these latter 19 animals, 14 were able to stand with the heel off the ground. There was no evidence of return of function of dorsiflexion of the toes in any of the animals after 30 or 45 days, but after 60 days 13 out of 22 animals no longer dragged their toes, but walked with a plantar gait.

In the animals with homogenous grafts there was no evidence of recovery 45 days after resection, but in the 60 day resected group 11 out of 17 animals walked with the heel off the ground. In the 75 day resected group 14 out of 14 walked in this same fashion but only 2 stood with the heel well off the ground. In none of these animals was there recovery of movement of the toes. In comparison, we noted that 7 out of 12, 180 day nonresected homogenous graft animals stood with the heel well off the ground, and 5 of the 12 walked with a toe drop.

MUSCULAR CONTRACTURES

In most instances the contractures found were mild, so that with a little tension the muscle could be stretched to its normal length. On the other hand a few contractures were quite obvious and no attempt to overcome them was successful, especially in view of the pain produced by the maneuver of the examiner.

As far as individual muscles are concerned, no significant contractures were found in the hamstrings or in the gastrocnemius muscle group; that is, the knee could be fully extended and flexed in practically all cases. The only exception to this was a rare instance in which a persistent draining sinus involved the hamstring muscle group. When changes were noted they were found in the anterior tibial muscles, in the common extensors of the toes, and in the plantar flexors of the toes. In the end-to-end sutures only 3 instances were found in 58 animals; 2 occurring in 60 day animals and the third in a 75 day animal. Two contractures were classified as mild and a third as severe, involving especially the flexor digitorum longus; this latter case being complicated by a persistently draining sinus tract from the bullet wound.

In the grafts of 45 days' duration no contractures were found in 8 animals, but after resection of the distal suture line 3 of these had mild contractures of the extensor digitorum longus at the end of the second 45 day period. In the 60 day group 2 mild contractures were

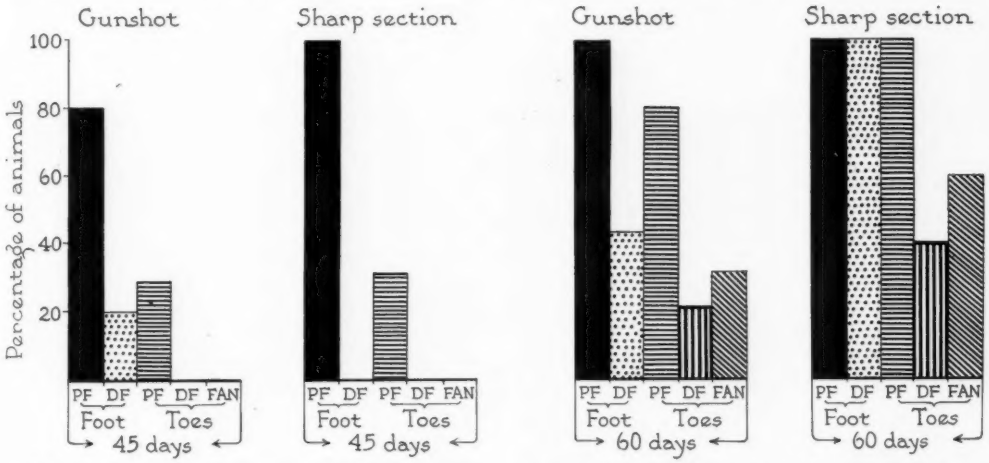

Fig. 20. Comparison of the response of the various muscle groups to direct electrical stimulation of the sciatic nerve 45 and 60 days after end-to-end suture. *PF*, plantar flexors; *DF*, dorsiflexors; *FAN*, abductors and adductors.

found before resection, but 60 days after resection 7 of the 17 animals showed mild contractures of the dorsiflexors of the foot and in 3 animals severe contractures of the flexors of the foot and toes were present, including two 90 degree and one 135 degree contracture of the flexor digitorum longus. In the 75 day animals with grafts, mild contractures were found in 5 of 14 animals before resection, while 75 days after resection 2 more showed mild contractures of the flexors of the foot and toes and 7 had a marked contracture of the anterior tibial muscle, 3 of which immobilized the foot at right angles with the leg. These animals also had a severe contracture of the flexor digitorum longus and in 5 of them the toes could not be moved from a flexed position, representing a 110 to 165 degree contracture. In the 12 animals with homogenous grafts allowed to go 180 days without resection of the distal suture line, there were but 2 animals with contractures of moderate degree.

MUSCLE ATROPHY

Sufficient data concerning muscle atrophy were obtained in only 25 animals of the gunshot series. In 3 animals with 60 day end-to-end sutures there was percentage weight losses of 51, 54, and 54, while 3 other animals with 75 day end-to-end sutures revealed percentage weight losses of 41, 49, and 50. These were large losses, but it must be remembered that these were very short experiments. This is more emphatically brought out when it is noted that a cat with a 15 month old end-to-end suture showed a weight loss of only 5 per cent. In the case of the homogenous grafts, 3 cats revealed percentage weight losses of 50, 54, and 54, respectively, 45 days after resection of the distal suture line, while the average of nine 60 day and four 75 day animals similarly treated were 51 and 58 per cent, respectively. Again this should not be considered a maximum in recovery since a cat with a 16 month homogenous graft, without resection of the distal suture line, had a percentage weight loss of but 7.5 per cent. A further interesting comparison can be made with the finding of an average weight loss of 15.5 per cent in 12 animals with grafts of 180 days' duration without resection of the distal suture line.

SIGNS OF SENSORY RECOVERY

In the animals with end-to-end sutures there were no instances of recovery to pin prick in areas of isolated supply up to 75 days.

In 4 of 9 animals 45 days after resection and resuture of the distal suture line of an homogenous graft performed 90 days previously, there was some return of sensation to pin prick in the area of isolated supply. A similar return occurred in 10 of 17 animals with 60

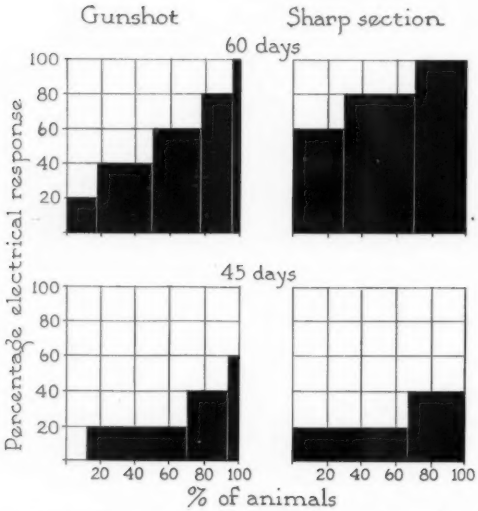

Fig. 21. Comparison of the percentage of muscular response to direct electrical stimulation of the sciatic nerve 45 and 60 days after end-to-end suture in relation to the number of animals manifesting this recovery.

day intervals and in 9 of 14 animals with 75 day intervals.

There was a complete return of sensation to pin prick at the end of 150 days in 10 end-to-end suture animals and at the end of 180 days in 12 cats with homogenous grafts in which the distal suture line was not resected.

Deep pain, or pressure pain, produced by compression of the toe pads was present in 33⅓ per cent of the animals 60 days after end-to-end suture; in 11.7 per cent of the animals with homogenous grafts in which the distal suture line was resected after 60 days, and the examination made 120 days after the graft had been originally introduced. In 14.2 per cent of animals with homogenous grafts, with a resected distal suture line at the end of 75 days, and studied 150 days after introduction of the graft, there was a return of pressure pain. However, 75 per cent of 12 animals showed a response after 180 days without resection and resuture of the distal suture line.

SIGNS OF TROPHIC DISTURBANCES

In 58 animals with short term end-to-end sutures only two plantar ulcerations were found. Both of these occurred in 60 day animals, one of which had a severe contracture together with a chronically draining sinus tract originating from the wound site.

In the animals with 45 day homogenous grafts, no ulcers were found in 10 animals before resection but one developed after resection. In the 60 day group 2 out of 17 animals developed ulcers before resection, while another 3 developed them afterward, giving a total of 6 out of 14 at the end of 150 days. In the series of 12 animals with homogenous grafts allowed to survive 180 days without resection of the distal suture line, only 2 ulcers were found, one involved the toes and the other the plantar surface of the heel.

RETURN OF REFLEXES

The step reflex was found in 40 per cent of the animals with end-to-end sutures of more than 25 days' duration. In only 3 of 33 animals with homogenous grafts of over 60 days' duration was there evidence of a step reflex, and this was a feeble response.

RESPONSE TO ELECTRICAL STIMULATION

Muscle responses to electrical stimulation were diminished in the case of end-to-end suture repair of severance by gunshot as compared with those of sharp division of the nerve.

The first observed response was plantar flexion of the foot. This was closely followed by the return of plantar flexion of the toes and dorsiflexion of the foot. Dorsiflexion of the toes and fanning of the toes were characteristically late findings although present in some animals at the end of 60 days.

After 45 days, the gunshot injuries showed a response of plantar flexion of the foot in 76 per cent of the animals as compared to 100 per cent of the sharp section injuries; plantar flexion of the toes, 23 per cent and 33 per cent and dorsiflexion of the foot 17 per cent and 0 per cent, respectively. In neither group was there a response of dorsiflexion of the toes or fanning of the toes. After 60 days, there was a 100 per cent response of plantar flexion of the toes in both groups; 77 per cent of the gunshot animals showed the response of plantar flexion of the toes as compared to 100 per cent of the sharp division experiments; dorsiflexion of the

TABLE I

Days	Percentage Recovery Gunshot—%	Sharp section—%
45	30.2	31
60	52.2	57
75	58.5	53

foot 27 per cent and 100 per cent; dorsiflexion of the toes 23 per cent and 40 per cent and fanning of the toes 32 per cent and 40 per cent, respectively (Fig. 20).

Another interesting comparison was found by noting the highest percentage of animals possessing the greatest degree of motor response upon electrical stimulation in each time period. In the gunshot series 6 per cent of the animals had 60 per cent return of function at 45 days and 4.6 per cent had 100 per cent return of function at 60 days, while the sharp section series showed 33 per cent of the animals with 40 per cent return of function at 45 days and 30 per cent with 100 per cent return of function at 60 days (Fig. 21).

In the homogenous grafts the average muscular response after resection of the distal suture line is shown in Table I.

Again, the same progression of recovery of response in relation to time was found in both series, but here it was noted that there was no great difference in the rate of recovery between the gunshot animals and the control series. This similarity is further brought out through the study of the breakdown of this recovery into terms of each function, as shown in Table II.

TABLE II

	45 Days		60 Days		75 Days	
	Gun shot %	Sharp section %	Gun shot %	Sharp section %	Gun shot %	Sharp section %
PFF	88.8	56	100	100	100	76
PFT	25.5	37	40.0	85	64	50
DFF	25.5	28	91	56	92	40
DFT	0	9	7	35	7.6	60
Fanning	13	0	20	21	28	30

PPF, plantar flexion of foot; PFT, plantar flexion of toes; DFF, dorsiflexion of foot; DFT, dorsiflexion of toes.

With regard to the highest percentage of animals showing the greatest degree of muscle response in each time period, in the 45 days resected distal suture line group 12 per cent showed 60 per cent return of function; in the 60 day group 17.6 per cent showed 80 per cent return; and 25 per cent of the 75 day group showed 80 per cent return of motion according to these criteria. This can be compared with

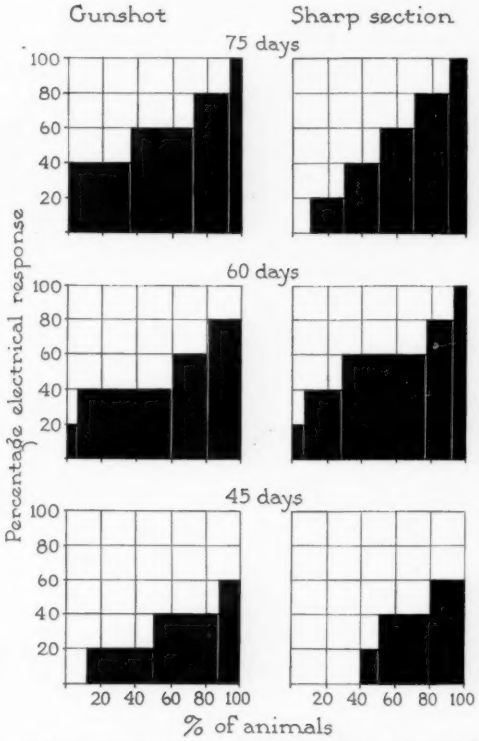

Fig. 22. Comparison of the percentage of muscular response to direct electrical stimulation of the sciatic nerve 45, 60, and 75 days after resection and resuture of the distal suture line of homogenous grafts in relation to the number of animals manifesting this recovery.

the sharp section series in which 20 per cent of the 45 day resected distal suture line graft animals showed 60 per cent of muscle response, while 7 per cent of the 60 day animals and 10 per cent of the 75 day animals showed 100 per cent return of response (Fig. 22). On the other hand, of 12 animals with nonresected distal suture line grafts of 180 days' duration, in the gunshot series, 60 per cent revealed 100 per cent muscle response upon electrical stimulation.

SUMMARY

1. Swelling is always present at the suture lines in end-to-end sutures as well as in autogenous and homogenous grafts. The distal suture line of a graft is always larger than the proximal suture line and it is larger in a homogenous graft than in an autogenous graft. It

is the result of the endoneural and perineural mesodermal proliferation which unites the severed nerve ends, or the graft, to the proximal and distal nerve segments. It precedes and complicates, but does not interfere, with the regeneration of the nerve fibers.

2. Trauma produced by handling and repairing the nerve causes a reactive epineural proliferation which is not only limited to the suture line but also involves the epineurium of the proximal and distal segment. Regenerating nerve fibers originating from the fanning out of fibers at the suture line are seen in large amounts in the proliferating epineurium as deviating and retrograde fibers. A traumatic zone is present for a short distance proximal and distal from each suture line, and is characterized by a necrotic degeneration of the myelin and of the axis cylinders resulting in an obliteration of the endoneural structure and the formation of Perroncito spirals. In this area the regenerating nerve fibers take a deviating course.

3. A very definite contusion effect within the nerve was found in the microscopic study of the gunshot injuries both with and without interruption of nerve continuity. Extensive traumatic damage was present in both proximal and distal nerve segments for a long distance away from the site of trauma. It leads to a process of necrobiosis and dissolution of the ectodermal elements with survival of the mesodermal elements. The pattern of nerve fiber regeneration which resulted was more confused than that of the usual suture line and accounted in part for the diminution of rate of early recovery of function.

4. Regenerating nerve fibers, preceded by Schwann cells, will follow the path of proliferating histiocytes, be it in the granulation tissue that fills the gap between the proximal and distal segments at the suture lines, in the proliferating endoneural sheaths of the degenerating distal nerve segment, the degenerated or necrotic graft, or wherever a histiocytic proliferation takes place around the suture lines or in the epineurium.

5. The formation of well developed axis cylinders and of myelin sheaths are observed in the distal segment of the nerve 45 days after end-to-end suture, although large amounts of myelin decomposition products are still present. Regenerating nerve fibers enter the suture line during the first 7 days after nerve suture.

6. Autogenous grafts and even more so, homogenous grafts, always appear thicker at the time of removal than at the time of transplantation. This increase in size is closely related to the amount of proliferated mesodermal tissue within and around the graft and also to the structure of the graft itself. More and denser adhesions are present around the homogenous than the autogenous grafts because there is also a more pronounced perineural and epineural mesodermal proliferation in the homogenous grafts. These adhesions carry blood vessels to the epineurium of the graft, the nerve segment, and to the suture lines.

7. Autogenous grafts are characterized by a predominantly isomorphous structure; that is, one in which the original neurilemma structure is preserved. The majority of homogenous grafts show a heteromorphous structure due to the destruction of the original graft structure which follows the necrosis of the ectodermal and endoneural elements after transplantation. Neurotization of autogenous grafts is predominantly regular and parallel to the graft structure while in homogenous grafts the regenerating nerve fibers follow an irregular and deviating course.

8. Despite the large amount of regenerating nerve fibers lost in the epineurium, the suture lines, and in the grafts of heteromorphous structure, the distal nerve segment always shows a satisfactory neurotization.

9. Muscle atrophy takes place in all operated-upon animals and the loss of muscle weight, when compared to the normal, non-operated-upon side, varies between 20 and 80 per cent. It recovers faster in cases of end-to-end sutures than following transplantation of a graft. The largest amount of muscle atrophy is present in the cases of homogenous grafts.

10. Motor function returns much earlier following end-to-end suture and remains better than after transplantation of an autogenous or homogenous graft. The first sign of motor recovery after a high sciatic nerve lesion

is plantar flexion of the foot, followed by plantar flexion of the toes and dorsal flexion of the foot. Dorsal flexion of the toes and fanning of the toes are late signs of recovery. Normal gait and stance involve a more complicated mechanism and appear late.

11. Sensory recovery tested by the return of pain sensation over the lateral and plantar surfaces of the foot, which form the area of isolated sensory supply, appears 60 days after end-to-end suture and 90 days after the transplantation of an autogenous graft. No critical sensory return could be found in the cases of homogenous grafts even 150 days after transplantation of the graft. The earliest response to deep pain is observed on compression of the 2nd toes 30 days after end-to-end suture and 90 days after repair by autogenous grafts.

12. Muscular contractures are more often seen in animals with homogenous grafts than in animals with autogenous grafts or end-to-end sutures. They occur during the stage of complete denervation as a result of the bad position assumed by the paralyzed extremity. The most common contractures involve the dorsiflexors of the foot and toes and the plantar flexors of the toes. Signs of motor recovery are observed in the contracted muscles as well as in the normal ones.

13. Trophic disturbances of the skin of the foot and toe pads and the claws are found in all the paralyzed extremities; their recovery is very slow. Trophic ulcers of the heel are present in 3.3 per cent of the animals after end-to-end suture, 6.2 per cent after transplantation of an autogenous graft, and 12 per cent following repair by homogenous graft. They develop during the period of denervation of the skin area, during the 30th and 45th day after nerve repair. They show poor healing tendencies.

14. Reflexes, such as the step and the fanning reflex, are very late signs of recovery and are rarely seen even 30 months after nerve repair.

15. Response to direct electrical stimulation of the repaired nerve is the most constant and earliest objective sign of motor recovery. It begins earlier and remains better in nerves repaired by end-to-end suture than by autogenous or homogenous grafts. Plantar flexion of the foot is obtained 45 days after end-to-end suture and plantar flexion of the toes and dorsiflexion of the foot 60 days after end-to-end suture; 75 days after transplantation of an autogenous graft; and 120 days after transplantation of an homogenous graft. Excellent muscle contractions could be obtained with a threshold current of 0.1 volt in most of the animals which did not show any, or little, return of function when tested by other methods. The difference in degree and kind of response to electrical stimulation and other clinical tests, between the nerves repaired by end-to-end suture, autogenous and homogenous grafts is probably due to the heteromorphous type of neurotization which follows the more complicated structures which prevail at the suture lines and in the grafts.

16. In gunshot wounds functional recovery as expressed by return of motion, return of sensation, and muscular response to direct electrical stimulation of the nerve was delayed following repair of the nerve by end-to-end suture. The extensive traumatic damage which takes place for some distance around the site of trauma and the resulting heteromorphous neurotization are responsible for the functional delay. No appreciable differences are present in the rate of recovery following the implantation of a homogenous graft in gunshot or sharp surgical wounds.

17. Clinical and experimental observations warrant that the operation of choice in cases of repair of an injured peripheral nerve in man, where direct end-to-end suture cannot be performed, is the transplantation of a nerve graft. The most satisfactory results are to be obtained by the use of autogenous grafts. If those are not available the use of an homogenous nerve transplant is justified.

THE SPREAD OF UTERINE AND OVARIAN CARCINOMA WITH SPECIAL REFERENCE TO THE RÔLE OF THE FALLOPIAN TUBE

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SINCE the sixteenth century, when Gabriello Fallopio gave the first clear description of the tubes that have come to bear his name, many years of observation have shown that the normal contractions of their muscular coat and the action of the ciliae of certain cells of their mucosal lining form a current from the peritoneal cavity toward the uterine cavity. This current may be reversed under certain conditions. With this knowledge at hand, it is strange that relatively little has been written on the transmission of carcinomatous cells by the lumen of the fallopian tube. It is known that uterine carcinoma sometimes involves the ovaries by means other than by direct extension and that malignant lesions of the ovary spread to the endometrium by equally obscure pathways. The purpose of this paper is to report the study of carcinoma arising in the ovaries or endometrium with reference to spread by way of the fallopian tube.

The rôle that the fallopian tube has played in the spread of carcinoma of the ovary to the uterine fundus and, conversely, in the transmission of carcinoma of the endometrium to the ovary has long been a point of controversy. Reichel, in 1888, reported 2 cases of primary carcinoma of the ovary with metastatic involvement of the endometrium. He expressed the opinion that the involvement of the endometrium was due to transmission of viable carcinomatous cells through the lumen of the fallopian tubes. Separate reports of free carcinomatous cells in the lumen of the fallopian tubes later were made by von Franqué, Morinaga, Sitzenfrey, Glendining, Clark and Norris, Schiller, Sampson (23), and Wallis.

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Abridgment of thesis by Dr. Lynch in partial fulfillment of requirements for the degree of M.S. in Surgery (University of Minnesota, 1943).

It is interesting to note that in many texts the advisability of performing curettage of the uterus, followed by implantation of radium in cases of carcinoma of the uterine fundus, is questioned because of the danger of disseminating carcinomatous cells through the fallopian tubes. This possibility of a retrograde flow has long been recognized. In 1924, Sampson (21) published the first of a series of reports in which he expressed the opinion that carcinomatous implants on the endometrium, mucosa of the fallopian tube, and serosa of the ovary had occurred as the result of transmission of viable cells by the aforementioned route.

Novak reviewed 147 cases of adenocarcinoma of the uterus and found 7 cases in which there was involvement of one or both ovaries. In 3 of these cases there also was tubal involvement. He found that the lymphatics had been invaded by malignant cells in all of the 7 cases and felt accordingly that lymphatic permeation, rather than transmission through the tubal lumen, accounted for the metastasis. In his review of the cases reported by Sampson he expressed the opinion that in some instances the proof of luminal spread was not adequate.

Many other reports have cited the concomitant finding of carcinoma of the ovary and the uterus, and some of the reports have mentioned tubal involvement (22, 24). Glendining, Boxer, Cameron, Norris and Murphy (15), Bernstein, Werner, Offutt, Norris and Vogt (16), and Robinson, have all observed one or more "combined" lesions in which the ovarian was thought to be the primary one. Norris and Vogt (16), Lynch, Cullen, Meigs, Crile, Offutt, Norris, and Dunne (14), Smith, and Stacy have reported cases in which carcinoma arose in the fundus of the uterus and metastasized to one or both ovaries. In many

instances it also involved the fallopian tubes. Most of the authors expressed the opinion that extension had taken place primarily through the lymphatics.

MATERIAL

This paper is based on a study of 113 cases of carcinoma of the uterus or ovary, or of both of these organs, that were observed at the Mayo Clinic in 11½ years, namely from January 1, 1929, to June 30, 1940, inclusive. This series does not include all cases of carcinoma of these organs that were observed at the clinic in this period; it includes only those cases in which operation was performed for removal of carcinoma of one or both of these organs and in which it was possible to study in a satisfactory manner the spread of carcinoma from the uterus to the ovary or from the ovary to the uterus.[1]

The 113 cases were divided into four groups. The criteria for this division will be considered subsequently.

METHOD OF STUDY

In studying this series of cases, the histories were first reviewed. The pathologic specimens then were examined grossly. Representative blocks of tissue next were cut from the endometrium, the ovaries, and the fallopian tubes. These blocks were embedded in paraffin, sectioned in the usual manner, and stained routinely with hematoxylin and eosin and by the Galantha method for mucin.

FINDINGS

Croup 1. This group includes 51 cases in which the carcinoma originated in one or both ovaries and metastasized to the fallopian tube but did not involve the endometrium. This is the largest of the four groups. It includes 45 per cent of the entire series of cases and 13 per cent of the cases in which the carcinoma originated in one or both ovaries. This is not surprising as the ovaries and fallopian tubes ordinarily are in close proximity and have common lymph channels. In many instances, the carcinoma spread by means of adhesive bands.

[1]In so far as it was possible examples of primary carcinoma of the fallopian tubes were deleted.

The average age of the patients was 44.7 years with extremes of 27 and 78 years. Ninety per cent of the women had been married but only 57 per cent of these had borne any children. Symptoms complained of varied in duration from 5 days to 4 years and included vaginal discharge, pelvic pain, and pelvic tumor. None of the symptoms were pathognomonic of the underlying disorder, although in approximately 10 per cent of the cases the presence of a bloody postmenopausal discharge seemed to be most easily explained by carcinomatous invasion of the fallopian tubes.

Bilateral ovarian carcinomas were present in 67 per cent of the cases, and in the majority of instances the grade of malignancy, as determined by the method of Broders, was high. In all except one instance the tubal extension was homolateral. In several instances tubal spread appeared to obtain on the basis of serosal "implantation." In all other cases, mural involvement was by direct extension or through permeation of lymph channels. No undoubted instance was found in which mucosal "implantation" alone obtained and in no instance were clumps of carcinoma cells found lying free in the lumen of the fallopian tube.

Group 2. This group includes cases of carcinoma of the uterine fundus with involvement of the fallopian tube (or tubes) but without metastasis to the ovaries. Twelve cases, or 3.2 per cent of the cases of primary uterine carcinomas studied, fulfilled the criteria established for this group. The average age of patients was 53.5 years, slightly lower than the usual figure cited in the literature for patients with carcinoma of the fundus. Extremes of 30 and 72 years were noted. Ninety per cent of the patients were married and the incidence of fertility was 90 per cent.

Symptoms were of the type to be expected in carcinoma of the uterus with no features indicative of tubal extension. Symptoms, on an average, had been present for slightly more than 1 year. Nine of the lesions were graded 1 or 2 (Broders' method), 9 had involved the fallopian tubes bilaterally, and 9 had invaded the tubal mucosa. However, in all 12 cases there was evidence of submucosal permeation in the lymphatic spaces with none demon-

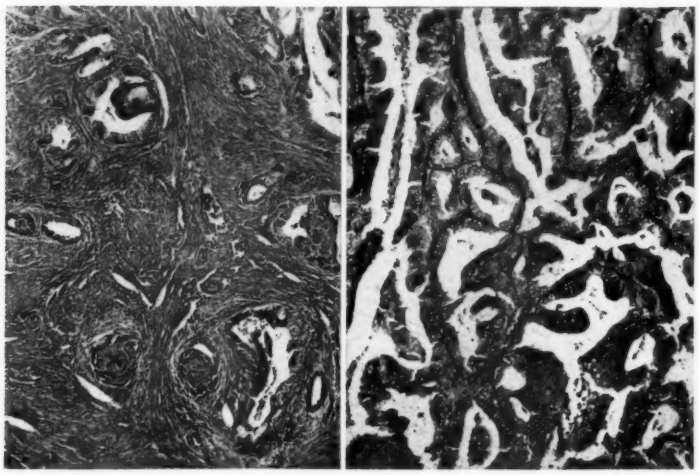


Fig. 1. a, left. Adenoacanthoma, grade 2, of uterus; a mixture of glandular and squamous epithelial elements is visible at *x;* section stained with hematoxylin and eosin (×50); b, metastatic adenoacanthoma of ovary; section stained with hematoxylin and eosin (×65).

strating evidence of spread via mucosal implantation exclusive of other methods.[1]

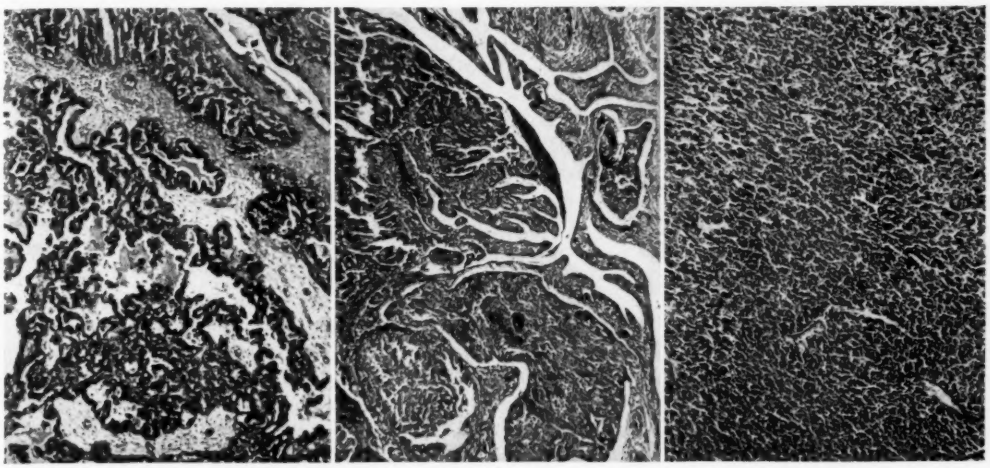
Group 3. This group includes cases of carcinoma of the ovary (or ovaries) and endometrium with involvement of the fallopian tube or tubes. In 20 cases, all of the aforementioned structures were involved. In 12 of these cases the primary growth was ascertained to be ovarian, in 6 it was uterine, and in the remaining 2 cases no decision could be reached in this matter. The average age of patients in the group was 51.1 years with extremes of 35 and 69 years. Fifty per cent of the patients had passed the clinical menopause. Symptoms present combined the features of those in groups 1 and 2. The symptoms had been present for an average of 17 months. The symptoms were not characteristic for this group of lesions.

Pathologically, the criteria used for indicting the ovary as the primary site of the malignant lesion were: (1) the size, degree of encapsulation and other gross features of the ovarian tumor; (2) the presence of papillary projections and of cysts; (3) the presence of psammoma bodies; (4) the demonstration of mucus; and (5) the finding of bottle neck cells which occasionally have caused pathologists to suspect primary involvement of the ovary in examination of malignant material curetted from the uterus. Conversely, the observation of rather well differentiated uterine glands of that peculiar mixture of glandular and squamous cell elements known among pathologists as "adenoacanthoma," indicated that the uterus might be the site of origin of the primary tumor (Fig. 1, a and b). Invasion of the myometrium, whether centrifugal or centripetal, was of some assistance in cases in which the site of origin of the primary tumor was doubtful. In some cases the occurrence of coexisting and independent uterine and ovarian lesions could be ruled out entirely.

All grades of malignancy were encountered; however, in general, lesions that occurred primarily in the ovary were potentially more malignant than were those that occurred primarily in the uterus. Bilateral tubal involvement was present in 50 per cent of the cases in this group. Unilateral involvement was equally shared by the right and left tube and extension from tube to ovary (or vice versa) tended to be homolateral.

The site of the tubal involvement was as

[1]Recently, however, 2 examples of such a mode of spread have been observed by one of us (Dockerty).



a b c

Fig. 2. a, Typical papillary cystadenocarcinoma, grade 2, of ovary, section stained with hematoxylin and eosin (×43); b, section of corresponding fallopian tube showing metastatic involvement, section stained with hematoxylin and eosin (×43); c, metastatic papillary adenocarcinoma, grade 2, of the endometrium (primary lesion was situated in the ovary), section stained with hematoxylin and eosin (×45).

follows: in 11 cases, the mucous, muscular, and serous coats were involved; in 6 cases, only the serous coat was involved; in 1 case, involvement of the muscular coat was associated with secondary ulceration of the mucosa, and in the 2 remaining cases the involvement was limited to the mucosa. With the possible exception of these 2 cases, the lesion appeared to have spread by direct extension or by lymphatic permeation or by both of these methods (Fig. 2, a, b, and c).

Group 4. This group includes 30 cases of carcinoma of the ovary (or ovaries) with concomitant carcinoma of the endometrium but without malignant lesions of the fallopian tubes. The average age of patients was 53.1 years with extremes of 41 and 70 years. Of 21 married patients 13 had borne children. Clinical menopause had occurred in 17 cases.

Symptoms complained of, as in group 3, shared the features of those of uterine and of ovarian carcinoma. They were rarely characteristic of the extent, to say nothing of the exact nature, of the pathologic lesions in the pelvis. The average duration of symptoms was 8.6 months.

The difficulties encountered in ascertaining the site of the primary growth were fully as apparent as they were in group 3, and the site was comparable in both groups. In 14 cases spread by extension, contiguity or lymphatic permeation accounted for the presence of identical lesions of the ovary (or ovaries) and the endometrium. In 11 cases the lumen of the fallopian tube seemed to play the part of a passive conduit for the transmission of carcinomatous cells without becoming secondarily invaded. In 4 of these 11 cases the lesions were primarily uterine. In 3 of these involvement of the ovaries took the form of surface implants and in 1 case there was invasion of a recently ruptured hemorrhagic cyst. In 7 cases a primary ovarian carcinoma spreading exclusively to the endometrium produced lesions that were diffuse in 2 instances and circumscribed and cornual in 5 cases. In all 7 cases penetration of the myometrium was minimal. In the 5 remaining cases it is quite possible that the ovarian and the endometrial lesions represented independent primary growths as their respective microscopic pictures differed somewhat.

DISCUSSION

It is the consensus, as gathered from the literature, that the uterus is one of the most

frequent sites of carcinoma among women. Malignant lesions of the uterine fundus account for 25 per cent of all malignant lesions of the uterus. Carcinoma of the ovaries has been found to represent 7.7 per cent of all gynecologic lesions by Norris and Murphy (15). Lynch has determined in his series of cases that 13.3 per cent of all malignant lesions of the pelvis arose primarily in the ovary. In our particular series of cases uterine (fundal) and ovarian carcinoma occurred with equal frequency. However, this does not take into account the cases in which the lesion was inoperable.

The incidence of multiple malignant lesions has been variously reported. In 1933 Hurt and Broders stated that in 3.4 per cent of a series of 2,124 cases the lesions were multiple. Warren and Gates (30) reviewed 1,259 cases of carcinoma and found multiple lesions in 1.04 per cent of the cases. White has concluded from his studies that in about 4 per cent of all cases of malignant lesions there is more than one primary site of origin, and that multiple lesions usually appear at an earlier age than do single lesions.

Offutt reported that in 8.6 per cent of 616 cases of papillary cystadenocarcinoma of the ovary, the lesion was associated with carcinoma of the uterine fundus. Offutt found concomitant lesions of the ovaries in 11.9 per cent of 512 cases of malignant lesion of the uterine fundus. Holland, in an examination of 10,000 fallopian tubes, found that 81 were involved by carcinoma. In 62 instances the growth was secondary to an ovarian neoplasm, while in 8 the primary focus was in the endometrium. Norris (15) found 8 instances of secondary neoplastic growth in the fallopian tubes in 2,000 gynecologic specimens. In 15 per cent of 759 cases of uterine and ovarian carcinoma in our series, extension was indicated by the criteria listed in the foregoing 4 groups.

Anatomic studies have demonstrated the existence of interconnecting links in the lymphatic drainage of the uterus, tubes, and ovaries. It is not surprising, therefore, that our studies have shown direct extension and lymphatic permeation as the chief pathways in the dissemination of carcinoma from one to the other of the aforementioned structures. The surprisingly small number of cases in which such modes of transmission did not hold revolve around the following crucial question: Does carcinoma spread by the lumen of an intact fallopian tube? Granted that it does, we can explain the occurrence on the surface of an ovary of a single metastatic lesion from, let us say, a primary adenocarcinoma of the uterine fundus. There is evidence in the case of Kruckenberg's tumor that the ovarian "peritoneum" like the general peritoneum may play host to the tumor implants. Similarly, in the case of ovarian carcinomas that occur among a relatively young group of patients, endometrial implants could be explained on the basis of implantation on a type of epithelium which is periodically breaking down and hence by no means intact. It is accordingly noteworthy that, in very few instances, was the mucosa of the fallopian tube involved by the implantation method. In almost all instances the phenomena of direct extension or lymphatic permeation or both were in operation. The inescapable conclusion is that carcinoma may spread from the uterus to the ovaries or vice versa. In the majority of cases the spread is by direct extension or by lymphatic extension or by lymphatic permeation alone or combined, and frequently, with simultaneous involvement of the fallopian tube as an intermediary stage in the process. In a minority of these cases viable malignant cells may spread through the lumen of the fallopian tube, usually without becoming implanted on its mucosa.

SUMMARY

In 113 cases of operative uterine and ovarian carcinoma the malignant process had invaded other pelvic structures: In 51, or 44 per cent, of the cases the lesion arose in the ovary and involved the fallopian tube, and in 12 cases it arose primarily in the fundus of the uterus and involved a fallopian tube. In 20, or 18 per cent, of the cases the lesion involved the ovaries, endometrium, and tubes. In 12 of these cases the primary site of the lesion was in the ovary, in 6 cases it was in the uterine fundus, and in 2 cases the primary site was doubtful. In 30 cases ovarian and endometrial

carcinoma coexisted without evidence of tubal lesion. The primary growth was uterine in 12 cases and ovarian in 13. In 5 cases the site of the primary lesion was doubtful and the possibility of two independent sites of origin could not be excluded entirely.

Approximately 6 per cent of ovarian carcinomas metastasized to the endometrium and examination of curetted material occasionally revealed the extrauterine site of the primary growth. Conversely, about 4 per cent of operable carcinomas of the uterine fundus eventually involved the ovary or ovaries. In both circumstances the fallopian tube seemed to act as the intermediary host to the malignant cells. In only 1.4 per cent of cases did it serve in the capacity of a passive conduit, and in only 0.4 per cent was the direction of the flow reversed, namely, from uterus to ovary. From a practical standpoint, therefore, little risk was indicated for the production of ovarian or abdominal implantation in curetting a uterus which is the site of a malignant lesion, prior to the insertion of radium. In only a few cases was evidence found that carcinoma cells became implanted on tubal mucosa in the extension of malignant lesions of the ovary or fundus of the uterus.

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THE EFFECT OF CONTINUOUS CAUDAL ANALGESIA UPON UTERINE MOTILITY DURING LABOR

A Study of Fifty Patients with the Lóránd Tocograph

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THE rapidly extending employment of continuous caudal analgesia in obstetrics has necessitated a closer study of the effect of this method, not only on mother and infant, but also upon the motility of the uterus. Opinion on this latter point is divided.

Both Gready and Hesseltine, and Lorhan, state: "The uterus appears not to relax, and appears to maintain its normal motility and mechanism."

Siever and Mousel, on the other hand, say: "The level of anesthesia should be kept halfway between the symphysis and the umbilicus; if it went higher progress of labor was impaired."

Hingson and Edwards (9) report: "When the analgesic agent is permitted to ascend to the higher levels of the thoracic peridural space there is diminution in the force and frequency of the uterine contractions with a retardation of the progress of labor noted."

To determine more accurately the effect of caudal analgesia upon the uterine contractions, the labors of 50 patients under caudal analgesia were studied by means of the Lóránd tocograph, an instrument devised for recording graphically the contractions of the uterus through the anterior abdominal wall (10, 12).

METHODS AND MATERIALS

The records of uterine activity under caudal analgesia were made between November 8, 1943, and April 8, 1944, upon 50 women in labor from the ward services of the Philadelphia General Hospital and the Kensington Hospital for Women, Philadelphia. The observations were recorded with the Lóránd tocograph. The closed circuit needle technique, as originally described by Hingson and Edwards (3), was used throughout. The anesthetic agent was metycaine 1.5 per cent in Ringer's solution.

From the Obstetrical Services, Philadelphia General Hospital and Kensington Hospital for Women. Thesis submitted to the Faculty of the Graduate School of Medicine of the University of Pennsylvania, toward the requirements for the degree of Master of Medical Science [M. Sc. (Med.)] for graduate work in Obstetrics and Gynecology.

After a 15 minute control period of recording and without removing the tocograph, the analgesic dose of metycaine was administered. The tocograph record was usually continued for an hour or more after complete analgesia was obtained. In each instance the level of analgesia was carefully checked. The level of analgesia was considered to be high when it went to the 4th thoracic segment or higher.

In midcaudal block the level of analgesia was below the 4th thoracic segment and above the 11th thoracic segment with complete relief from the pain of uterine contractions.

Low caudal block existed when the analgesia did not extend high enough to relieve the pain of uterine contractions but involved sacral and lumbar segments only.

RESULTS

The tracings obtained from 50 patients in labor were evaluated according to the effect of the analgesia upon the strength and frequency of uterine contractions and on the uterine tone.

Contractions. Of these patients 33 demonstrated no significant change in either strength or frequency of contractions (Fig. 1). In 9 patients the contractions were interrupted for periods of 30 minutes to 2 hours (Fig. 2).

Six patients exhibited a decrease in frequency of contractions, and 1 a noticeable decrease in the strength of the contractions (Figs. 3 and 4).

Two patients showed significant improvement in both the strength and frequency of contractions (Fig. 5).

Tone. Of the 50 patients studied 27 showed no change in uterine tone during analgesia. However, 22 patients exhibited a progressive decrease in tone, and 1 exhibited a marked rise in tone (Figs. 6 and 7).

OBSERVATIONS

Analysis of the results obtained in this study indicate that the most important factor influencing the motility of the uterus under caudal analgesia was the height to which the analgesic level was permitted to ascend.

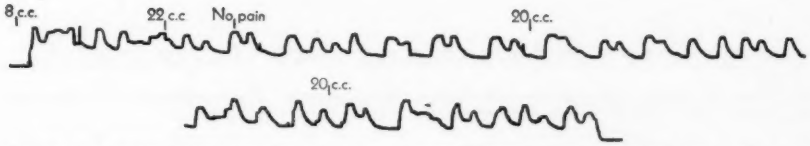

Fig. 1. This record is typical of the 33 patients in whom labor continued without change in strength or frequency of contractions. Complete relief from pain was attained at the position marked "No pain."

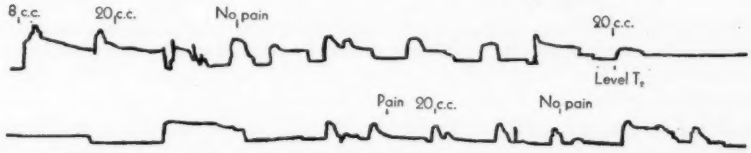

Fig. 2. Illustrated interruption of uterine contractions for 40 minutes when level of analgesia was permitted to ascend to the level of the second thoracic segment. Note absence of contractions when level reached *T2* and spontaneous return of contractions when level fell to symphysis pubis.

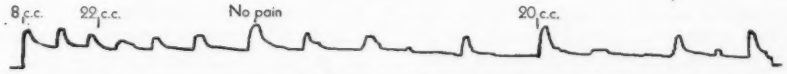

Fig. 3. The progressively increased interval between uterine contractions may be observed. Six patients exhibited similar mild decrease in the frequency of contractions.

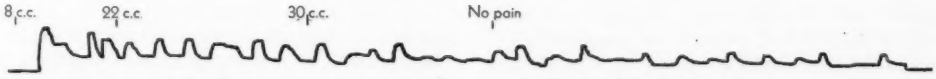

Fig. 4. This patient exhibited a noteworthy decrease in the strength of uterine contractions. Note the smaller amplitude of the later contractions as compared with those in the control period.

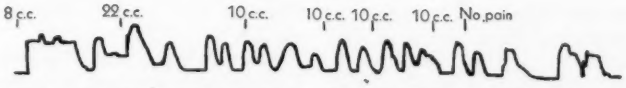

Fig. 5. Marked increase in strength of uterine contractions observed under low caudal block. Note tiny contractions of the control period. Also 4 additional doses were required to raise analgesic level and relieve pain.

Each of the 9 patients in whom labor was interrupted had a level of analgesia above the 4th thoracic segment. When the level was allowed to fall, labor started again.

The 2 patients in whom contractions were increased in strength had levels of analgesia involving the sacral segments only. These women complained that the pains were made worse and the tocograph records showed significant increase in the strength of the uterine contractions. When the analgesic level was subsequently raised above the 11th thoracic segment and the pain relieved, the stronger pattern of contractions persisted.

In 35 patients levels of analgesia between the 6th and 7th thoracic segments were attained. Of these patients 7 recorded minor changes in the strength or frequency of contractions. These changes were not sufficient appreciably to lengthen the labor. The remainder of these patients recorded no change.

The remaining 4 patients numbered those in whom labor was not interrupted even though the analgesic levels were above the 4th thoracic segment (Fig. 8).

That labor may often be interrupted by analgesia above the 4th thoracic segment of the cord would seem to indicate that the motor fibers to the uterus leave the cord in this area. This is in accord with the findings of Cleland and of DeLee who observed that the motility of the pregnant uterus was not interfered with even after transection of the cord at the level of the 6th thoracic segment.

Hingson (8) has used this principle in the management of 4 patients with premature labor induced by accidental trauma. High caudal block

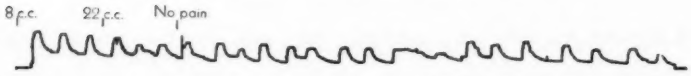

Fig. 6. Note that the record runs progressively downward. This represents a fall in uterine tonus which occurred in 22 patients. The significance of the decrease in uterine tonus is as yet unexplained.

Fig. 7. The record of one patient with an unexplained rise in tone. It should be noted as possibly significant that the rise in tone occurred when only a low caudal block was attained and before complete relief from pain.

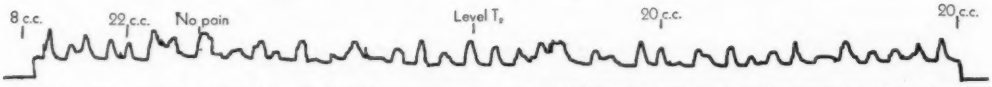

Fig. 8. The record of one of 4 patients is presented in whom a level of analgesia above the 4th thoracic segment was attained without causing interruption of uterine contractions.

was maintained for about 12 hours during and following which there was complete cessation of labor. Three of these patients went on to term; the fourth went 3 weeks past term, and all were delivered of normal babies.

Four patients received high caudal block above the 4th thoracic segment without noticeable change in their labor. This is not explained adequately. The varying thickness of myelin sheaths in different nerves and individuals as shown by several observers (4, 6, 7) may be a factor.

Two patients in whom sacral block only was attained showed increased labor. This might indicate that the parasympathetic fibers of the sacral nerves, in addition to their function of maintaining the tone of the smooth muscle of the cervix, may have an additional function of inhibition of the remaining uterine musculature. Removal of this inhibitory influence may account for the improvement in labor.

The significance of the diminution of tone observed in 44 per cent of patients studied is not explained. However, clinically it does not appear to be equivalent to the relaxation of the uterus produced by deep ether or chloroform anesthesia, considered necessary for intrauterine manipulations such as podalic version or decomposition of frank breach. We do not believe it sufficient to relax a contraction ring.

SUMMARY AND CONCLUSIONS

A Lóránd tocograph was used to record graphically the labors of 50 women receiving continuous caudal analgesia.

The most important factor determining the effect upon the uterine motility was the level to which the analgesia ascended.

When the recommended level (between the 6th and 10th thoracic segments) was maintained, only 20 per cent showed any decrease in uterine motility, and these were very minor changes. The remainder were unaffected.

When the level of analgesia was permitted to ascend above the 4th thoracic segment, 69 per cent of the patients had their labors interrupted.

When a low level of analgesia involving only the sacral nerves was achieved in 2 patients there was a marked improvement in the strength and frequency of the uterine contractions. This improvement continued after relief from pain was attained.

Forty-four per cent of patients studied showed a progressive decrease in uterine tone. This did not appear related to the level of analgesia.

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PILONIDAL CYST AND SINUS, THEIR MANAGEMENT AND OPERATIVE TREATMENT

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THE prevalence of pilonidal cyst and sinus has been repeatedly brought to the attention of the medical officers in the armed services and various phases of military life have been charged with precipitating activity, inflammation, and infection in these lesions. Authors, for the most part, have tabulated formidable numbers of postoperative sick days in their individual series, many of them presenting 35 sick days or more per case, and there are numerous instances of patients still being unhealed as long as 100 days after operation. Failure to obtain primary union regularly after suture of the wound is reported and, largely for this reason, various efforts to achieve some compromise with what is admittedly the ideal of primary closure have been formulated. A measure frequently recommended is closure of the skin margins to the sacrococcygeal fascia after complete excision of the lesion and its surrounding bed of fat. Another method that has its advocates is the removal of only the most superficial portion of the cyst and the marsupialization of the remainder by suture of its margins to the skin in the expectation that the exteriorized cyst wall will assume the characteristics of normal skin.

The length of time which must elapse before a patient can return to full duty after these procedures is still far greater than in those in whom primary union has been achieved. If they are to be adopted as routine measures, i.e. as suitable for the average case in the young men who make up the overwhelming majority of the patients reported, it is necessary to assume (1) that there is no practicable alternative to prolonged disability in order to assure cure, (2) that the final result will be satisfactory in a high percentage of cases after such procedures, and (3) that excision and primary suture, while ideal, cannot be accomplished with great regularity. It is the writer's belief that none of these assumptions can be safely made and his own experiences with such lesions in 38 consecutive admissions over a recent period of 18 months are offered herewith in substantiation of that opinion. Personal conversation with other surgeons in both of the armed services and observation of their patients convince the writer that his results are in no way unusual.[1] The fundamental principles on which those of us who have routinely practiced primary closure after excision are agreed are presented for consideration, together with an outline of points of management and operative technique. It is only fair to state, as have all other authors presenting data on such operations on military and naval personnel, that the final results in respect to recurrence will rarely become known to the operator himself. It can reasonably be expected, however, that the application of a given method to military personnel should yield substantially the same recurrence rate as that formerly encountered in civilian practice, unless the average lesion in the former prove to be more severe. In the experience of the writer, the reverse has been true, seriously complicated cases being less common in these relatively young patients than among civilians applying for surgical treatment.

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PERSONAL CASES

There was a total of 38 admissions to the sick list involving 34 patients with the diagnosis of cyst, teratoma, sacrococcygeal, in a period of 18 months. (The incidence is interesting in relation to the total of operative cases

[1]As these results were being tabulated, a paper by Ralph V. Byrne, Lieutenant Commander M.C., U.S.N.R., appeared in the *U. S. Naval Medical Bulletin*, 1944, 42: 386–389. He reports excision and complete suture in 20 of 23 patients, with primary healing in 17. The average healing time was 16 days, the longest being 30 days. The author's views, in general, are almost identical with those developed in the present publication.

for this period, to be reported later, numbering slightly over 500.) Of the 38 admissions, inflammation was present in 24 cases and absent in 14.

The term, inflammation, has been applied, rather than infection, in this compilation only because the former is in accord with the system of nomenclature of the Medical Department of the Navy. The great majority of the 19 patients presenting acute inflammation had frank abscesses in the cyst which had perforated the deep layers of the skin on admission and had, in a few cases, established inadequate drainage. Of the 14 patients who were treated by incision, this operation was done within 24 hours of admission and the quantity of pus was estimated to be 1 ounce or more in 9 instances. Organisms in abundance were invariably present in stained preparations of direct smears. The only patient not operated on was a straggler who had established adequate drainage spontaneously and whose inflammation was subsiding on admission. He refused excision after 5 days of treatment and was sent on to his own activity to await disciplinary action and eventual excision of the cyst. In 4 patients the acuity of the inflammation was so early, or began to subside so promptly after admission, that excision of the lesion was done in from 1 to 8 days.

Of the 5 patients showing chronic inflammation and purulent discharge on admission, 3 had not been free of discharge for longer than a week at a time for over 10 months. Treatment to minimize infection and decrease drainage was carried out for a maximum of 6 days before excision. One patient showed moderate local improvement on treatment for 12 days, but a generalized pyoderma which had developed after incomplete excision elsewhere of his cyst some 3 months previously proved to be so indolent that he was transferred to a naval hospital for further treatment.

Of the 14 admissions (13 patients) without current inflammation, there was a past history of acute inflammation in 12. In 7 cases, incision had been done on from 1 to 4 occasions; it had been carried out at our activity in 3 cases. One patient was a readmission with a small sinus persisting after excision 10 weeks previously by the writer. Excision of the lesion was done within 2 days of admission in all these cases.

It should be clear from this presentation of the past history and condition on admission of the patients that no asymptomatic cysts or blind sinuses were operated upon. All of these patients had lesions which were, or had been, incapacitating. A history of previous incision on from 1 to 4 occasions was given by 14 of the patients. It was impossible to decide in which of these instances an effort at excision had been made.

Further comment on the 14 patients on whom incision was done on admission is pertinent. Incision was performed on the day of admission in 10 instances, on the following day in the remainder. Sulfathiazole, 5 grams, by mouth daily, was started on admission and continued for the few days that the patient remained on the sick list. The decision to leave a soft, rubber drain in the incision was made on the basis of the size of the cavity and its depth. Even though pus was under pressure in all these cases an effort was made to express all the free necrotic material at operation, the wound being spread open by a hemostat and all hair and semisolid material lifted out. The tendency was increasingly toward the use of an incision between 2 and 3 centimeters in length in order to obtain prompt evacuation of the contents of the abscess, rather than the use of a small stab wound which would serve only to relieve tension. The drain was removed in from 1 to 3 days, by which time the discharge was small in amount and largely serous in nature. It was not necessary to reopen any of the wounds. Three of these patients were subsequently readmitted for excision. A circular block analgesia of the full thickness of the skin was employed in nearly all cases. The common practice of using ethyl chloride spray for topical analgesia has been long since abandoned by the writer as being inadequate to permit the procedures outlined here. The problem is not at all the same as that involved in draining a furuncle. If all foreign material, particularly hair, is not removed at the time of incision, these wounds will continue to drain intermittently and remain inflamed for months. The avoidance of a foreign body reaction permits prompt heal-

ing and early return to full duty pending excision at whatever time is convenient.

Among the 22 cases in which excision was done there was one with a shallow (2 cm.) sinus persisting some 11 weeks after excision *en bloc* of skin, fat, and fascia and primary closure by the writer, the only known "recurrence" in this series. Excision *en bloc* through double elliptical incision of skin, fat, and sacrococcygeal fascia was the technique employed in 7 instances. These were among the earliest cases in this series and followed the previous custom of the writer in civilian practice. Routine section of these blocks of tissue operated on in a quiescent phase, however, revealed the characteristic lesion to be a surprisingly small cyst, 2 to 3 centimeters long in its greatest diameter, invariably superficial to the fascia and rarely having secondary sinuses.

On the basis of these observations it seemed obvious that a wholly unwarranted sacrifice of normal tissue, with consequent difficulty of closure, was being made by the employment of block dissection in the average case, even though an incision only some 6 to 8 centimeters long and of a maximum width determined by the palpable margins of the cyst was used. It was decided to continue to define the lateral margins of the cyst at their attachment to the skin, then to follow the cyst wall by dissection, removing only such skin and fat cephalad and caudad to the lesion as was necessary to outline a skin incision of the necessary length in proportion to width for easy closure. This would result in the sacrifice of only a few millimeters of fat lateral to the cyst and to a depth of less than 1 centimeter elsewhere. It would be necessary, of course, to distinguish among strands of tissues of three types during such an enucleation excision, any of which may be seen to blend with the fibrous capsule about the cyst wall: (1) blood vessels, (2) fibrous tissue reflections of the sacrococcygeal fascia, (3) epithelium-lined tracts. It is the writer's contention that the surgeon operating upon such cysts in a quiescent phase should be able to make this gross differentiation. Such was the technique employed in the 14 operations listed as enucleation excision.

The validity of these observations and assumptions was borne out by the finding of secondary sinuses in only 2 of the 21 patients subjected to primary excision; in only *one* of them was the wound packed open to await healing by granulation. Fibrous strands were occasionally followed down through the fascia, particularly along the coccyx, and the cyst was rarely as large as the end of one's thumb. Primary closure in layers without tension and without the necessity for the mobilization of fat was relatively simple except when the cyst lay rather high in the sacral region where the fat pad is thinner than elsewhere. These patients may be fairly regarded as being an average, run-of-the-mill group as they are seen in the young men of the armed services.

A point of technique that the writer has not seen advocated is the incision of the skin obliquely, rather than at right angles to its plane, throughout the length of the incision, in order to assure perfect coaptation of skin edges in closure during which both margins of the wound are rolled toward the midline with resulting inversion of the skin if the latter is incised at right angles to its surface. Closure of the fat not only from side to side, but with attachment by suture to the fascia is essential to the obliteration of dead space. The writer prefers suture of the fat by one or two rows of fine material, of whatever nature, to its closure with the skin by through-and-through sutures. A small, soft rubber drain was placed to the depth of the wound in 13 of the 20 patients in whom primary suture was done and was removed on the first day after operation in 8 of these. Only a wound of this region in which hemostasis is literally perfect should be left undrained. Since all excisions were done under circular (field) block analgesia with 2 per cent procaine, the risk of delayed bleeding, though minor in amount, seemed to make this precaution against hematoma formation worthwhile. This type of analgesia is ideal, though time consuming, as no distortion of the tissues in the operative field occurs, as would be the case with infiltration. There is no objection to the use of spinal analgesia for this purpose. The wound surface was usually "frosted" very lightly with crystalline sulfanilamide before closure of the wound was carried out and a compression dressing was applied routinely.

Primary healing was obtained in 18 of the 20 cases in which complete suture of the wound was done. The 1 partial failure occurred in a patient in whom excision of a large cyst located higher on the sacrum than usual was performed on the 6th day of treatment, earlier than would have been ideal in view of the considerable induration about the cyst and the profuse purulent discharge from 2 of his 4 midline sinuses on admission. Incision had been made elsewhere 10 months previously and drainage had been almost continuous thereafter. The field was still too vascular, due to lingering inflammation, for good hemostasis at the time of operation and there was sufficient induration of the tissues to make approximation difficult even after mobilization of the fat layer. The comment was made that the choice between packing the wound and attempting closure was probably an even one. A hematoma in the lower third of the wound was drained on the 4th day and mild wound infection supervened, yet the upper two-thirds of the closure held securely and healing of the lower third by secondary intention was complete on the 31st day, a decided saving of time over what could have been expected had no closure been attempted. The occurrence of a persistent, superficial sinus in one other case, with eventual reoperation, has been referred to.

Patients were discharged under treatment on an average of 4 days after simple incision, with a recommendation for light duty for a period of one week. If, at the end of this period of light duty, the man was to be transferred to another activity, the recommendation was made that excision of the lesion be done after a further interval of 6 to 8 weeks. The usual immediately postoperative care involved sulfonamides orally, as previously noted, local heat and sitz baths twice daily following removal of the drain until the wound was free of discharge, ordinarily on the 4th day. No probing or other exploration of these wounds was done. It was not necessary to extend the period of light duty in any case. Three of these patients returned for excision of the lesion at intervals of less than 10 weeks. None had had pain or discharge in the interim. An interval of perhaps 6 weeks between incision of a grossly infected cyst and its excision is ideal, though frequently not practicable. When the interval is less than 3 weeks, the remaining induration and increased vascularity make both accurate dissection and closure noticeably more difficult and healing is impaired.

The longest period to complete healing in the 22 patients whose lesions were excised was 43 days. This patient in point was the only one for primary excision in whom packing of the wound was employed. The other patient in whom closure was not made has been previously referred to. He was completely healed in 10 days after secondary excision of a small, persistent sinus. The second longest interval between operation and healing, 31 days, has also been alluded to as occurring in the other patient in whom complete primary suture was partially unsuccessful. All other patients were discharged from the sick list, completely healed and fit for duty in 15 days or less after excision, the average being 12.7 days. No recommendation for light duty was made in these cases.

Postoperative infection was not a factor of consequence in this series of patients. In only 2 patients was purulent drainage from the wound present after excision, though slight redness about the skin sutures was not uncommonly seen. The postoperative regimen followed with rare exception in these patients involved: (1) a minimum of 10 days' strict confinement to bed; (2) the avoidance of lying on the back during this period, (3) clear liquid diet and paregoric for 3 days after operation and a low residue diet and mineral oil daily thereafter; (4) the administration of pituitrin to induce the first bowel movement on the 4th or 5th postoperative day and the avoidance of an enema at any time; (5) the initiation of oral sulfathiazole therapy, 5 grams daily, if redness developed about the sutures; (6) careful, regular cleansing of the wound area, gluteal cleft, and perianal skin to maintain dryness of these tissues. Alternate skin sutures were usually removed on the 7th day, the remainder on the 9th or 10th day. Sutures about which there was slight necrosis were not removed before the 10th day but were allowed to cut through the tissues. The buttocks were kept strapped together lightly

for 10 days and healing of the incision per primam was almost invariably complete at this time. Incidentally, it is a common paradox to find that the surgeon has strapped the patient's buttocks together but has maintained the patient in the supine position. The two measures, as explained, produce mutually antagonistic effects on the wound. A few days of increasing activity after being allowed out of bed was sufficient for the necessary regaining of strength, particularly of the legs, in these young men before they were returned to duty. The opportunity of "shore liberty" was a powerful incentive to complete recovery.

The writer regards the practice of allowing these patients to be ambulatory before the 10th postoperative day as an invitation to wound complications, regardless of the suture material used and the method of its insertion. If one will have a patient who already has a disruption of the lower end of his wound sit on a stool, inspection of the wound in this posture will reveal that the defect has assumed a greater dimension transversely than vertically; and any posture that tends to flatten the buttocks exerts a disruptive stress on the incision. Even though buried sutures be not actually broken or pulled out of the tissues, such a stress can only tend to form dead space in the wound with subsequent serum collection. The early removal of skin sutures leaves the skin itself without any strength to resist separation and if through-and-through sutures are depended on for closure, only a plastic exudate holds the entire wound together for the first 10 days, if the sutures are removed before true fibrous tissue is laid down in healing. These are simple fundamentals of wound healing which apply to any wound that tends to burst on stress rather than to close itself, as in the case of a muscle-splitting incision. The writer has seen these principles violated repeatedly with predictably poor results. In this particular operative field, all the tissues are normally under tension, and excision of these layers inevitably increases the tension on all layers after suture. Dead space, once formed, is rapidly filled with serum, and if it does not break through the superficial closure before the patient is dismissed from medical observation, it remains more or less encapsulated and acquires a chronic granulation tissue base. Breaking down of the wound weeks after discharge from the sick list may then occur and the lesion is improperly labelled a recurrence, with the implication that some portion of the cyst or sinus had not been excised.

Personal inspection of a few patients who have had a partial closure by the compromise method of suture of skin margins to the sacrococcygeal fascia, leaving a space between to granulate in the hope of eventual epithelization, has revealed unsatisfactory late results, although all of the patients examined had been returned to a duty status on the assumption that they were fit for duty. They were usually still unhealed after months on the sick list and all complained of pain on sitting. This procedure disregards the fundamental necessity for a scar of normal thickness to cover the sacrum, a necessity familiar to all who have had experience with posterior resection of the rectum by the Kraske method. Suture of the skin margins to the fascia, leaving the intervening space free of fat, precludes the possibility of any but a thin scar. With due regard for the fact that these patients who still complain of pain and tenderness become labelled as gross exaggerators after 3 or 4 months, all previous surgical experience indicates that they will be made comfortable by a plastic procedure which involves mobilizing a pad of fat and skin over the sacrum. Fat is perhaps sacrificed at even greater cost than skin in this region.

The writer has not had the opportunity of examining patients after the "marsupialization" procedure previously referred to, but is not aware of the validity of the evidence for the claim made that the remaining portion of cyst wall will assume the characteristics of skin. Finally, laying open sinuses and cysts that have given symptoms, from nearly all of which micro-organisms can be cultured, as a preliminary to excision makes closure hazardous, due to the likelihood of contamination of the field. There is a coincidence between advocacy of such preliminary exploration of the cyst and of a compromise with the ideal of primary closure which suggests that this risk has been widely appreciated. Marsupialization does, in fact, offer a means of removing

some portion of an inflamed cyst, rather than simply draining the abscess, but that it has any place as a routine procedure for the average case is by no means clear from the published data. The length of time reported per case is in excess of that following successful primary closure and the assurance of a comfortable, dry scar as a final result awaits the publication of late observations on these patients.

SUMMARY

Recently published experiences with excision and primary suture for pilonidal cyst and sinus indicate considerable dissatisfaction with the results, although it is generally agreed that this is the ideal procedure.

Various substitute measures which compromise with either complete excision or complete closure of the wound have been advocated as routine operations. They involve, however, a prolonged period of healing and uncertainty of ultimate result, the reasons for which have been discussed.

The writer believes that the average severity of the lesion as seen in members of the armed forces is less than that usually encountered in civilian practice and he has continued to use complete excision and primary suture as the routine procedure unless a frank abscess is present. Analysis of his operative cases over a recent 18 month period reveals an average of less than 15 postoperative sick days for the 22 patients in whom excision was done, complete closure of the wound in 20 patients and the achievement of primary union in 18 of these with less than 13 sick days per case after operation.

Enucleation excision, removing a minimum of healthy tissue, has been done in a majority of the cases, rather than excision *en bloc*, and contributes importantly to the ease with which the wound may be closed.

Fundamental considerations of management and technique are presented as essential to achieving an ideal result in a reasonable percentage of cases.

MULTIPLE CARCINOMAS OF THE LARGE INTESTINE

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WHILE multiple cancers of different or of paired organs are no longer looked upon as biological curiosities, multiple malignant tumors of the large intestine have been reported infrequently. This subject presents many interesting controversial aspects particularly with reference to cancer immunity, longevity, and origin. There are many reports on synchronous and metachronous cancers in different organs, but the literature is sparse in its treatment of multiple carcinomas limited to the large intestine. The multiplicity of malignant lesions in this location presents problems of diagnosis and treatment that differ from dual lesions elsewhere. This investigation is limited to cancers in the colon and rectum as encountered during the years 1934 to 1943 inclusive.

IMMUNITY AND MULTIPLE CARCINOMAS

Gaylord, Clowes, and Baeslack, in 1905, noted that, in animals inoculated with the Jensen rat tumor, regression frequently occurred. Once recovery took place these animals were insusceptible of reinoculation. These observations were corroborated by Michaelis, Borrel, and Ehrlich, and led to the theory that active immunity could be established by the inoculation of tumor tissue. It was soon apparent that such resistance while most pronounced against the specific tumor used extended to other growths to a lesser degree. Ehrlich broadened the theory considerably by concluding that resistance thus produced was universal (pan immunity).

Based on experimental transplantation of malignant cells in mice, he stated that one cancer furnished immunity to the subject against any additional primary cancers. This immunity may be acquired or natural. Although one group of mice may be resistant at all times to transplantation of a specific tumor tissue, others at first may be resistant. With repeated applications, successful "takes" eventually can be obtained. If the mouse with a successful transplant can overcome the growth, or if the tumor tissue be removed, a permanent immunity may be established in that mouse against further inoculations of that same specific tumor tissue. Maud Slye was never able to induce cancer in mice resistant by heredity. In mice susceptible to cancer in a specific location, she was never able to produce a malignant growth in other areas in spite of repeated trauma. Boyd maintained a similar view that immunity against the appearance of a second cancer is conferred on the subject by the presence of a malignant neoplasm. For this reason he stated that multiple cancers are very rare.

Ewing believed that the presence of more than one carcinoma in the same or in different organs of the same patient was nothing more than the "accidental coincidence in several organs of the biological factors in the genesis of tumors." Fried, finding only one case of multiple cancers in one thousand autopsies, Hanlon and Orr agreed that their occurrence is only coincidence.

Peller, by artificial production of easily curable and harmless skin cancer, claimed to have created immunization against visceral cancer. Confirmation of his work was advanced by Schmidt, who, in a study of multiple malignancies based on thirty-seven hundred consecutive necropsies, did not find a single visceral cancer combined with a skin epithelioma. However, he concluded that it would be wishful thinking to assume that in order to prevent visceral carcinoma one need only to acquire artificially an easily curable skin malignant lesion.

In the experimental laboratory, Bonser and Wainman found that no antagonism existed in mice between the presence of a malignant tumor in one organ and the appearance of a second cancer in another.

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TABLE I.—AVERAGE AGE IN SINGLE CARCINOMA OF THE LARGE INTESTINE (1934–1943 INCLUSIVE)

	Male	Female	Total
Colon	82	77	159
Rectum	103	82	185
Total	185	159	344
Percentage	53.8	46.2	100

Average age—56.1 years

LONGEVITY AND MULTIPLE CARCINOMAS

The belief was held by several investigators (Hanlon, Orr) that, as a result of earlier diagnosis and treatment, the survival period after the removal of a cancer permitted more time for the development of a second malignant growth. Hanlon, in 1931, ascertained that 3 carcinomas occurred in an age group that averaged 63.6 years, that 2 cancers existed in a younger age (58.8 years) as compared with the average age (58.4 years) for single carcinomas. Warren and Gates, in an excellent critical survey and statistical study of the literature to 1932, collected 1,259 cases and concluded that both multiple and single malignant tumors occur at about the same age and that any statement that the former occur at a more advanced age is contrary to the facts.

CRITERIA

Billroth, in 1869, reported the first case of multiple carcinomas and offered certain criteria which he felt had to be satisfied before the authenticity of a multiple cancer could be established. The postulates are that each tumor must differ histopathologically; must arise in a different location; each must be responsible for its own metastases. These criteria, while applicable to multiple malignant growths in different organs cannot apply to those arising in the large intestine. It would be difficult to demonstrate histopathological differences considering that the tumors arise from similar epithelial cells. Nor can the third postulate be followed for reasons related to the above. Moreover, with early diagnosis and treatment, metastases are frequently absent. Therefore, the more liberal criteria suggested by Warren and Gates have been adopted for this study. They are that each tumor must be malignant, distinct, and one lesion cannot arise as a metastasis from the other.

TABLE II.—AVERAGE AGE IN MULTIPLE CARCINOMA OF THE LARGE INTESTINE

	Two	More than two
Collected cases (Warren and Gates)..		11
Collected cases (1933–1943).....	66	6
Jewish Hospital series (1934–1943)...	13	3
Total.....	79	20
Average age.....	54.8 yrs.	51.9 yrs.

CASE STUDY FROM THE JEWISH HOSPITAL (1934–1943)

This investigation is based on all carcinomas of the colon and rectum as encountered at this hospital during the 10 years (1934 to 1943). All are of proved malignancy, the tissue having been obtained by biopsy, laparotomy, or autopsy. In this period there were 344 patients with cancer of the large intestine. Of these, 16 (4.6%) had multiple, malignant growths. This incidence is about the same as that reported by many authors for multiple carcinomas in different organs. In three thousand surgical cancer cases, Owen found the frequency to be 4.7 per cent. Ward reported an even higher incidence, 5.2 per cent, in a series of 1,773 cases of skin cancer. In a collected series of 29,740 patients with carcinoma, Warren and Gates found the incidence to be 1.84 per cent. The few reported series of multiple malignant growths limited to the large intestine reveal a much lower incidence than we experienced. Thus, Brindley had 8 patients in a total of 306 cases (2.6 per cent). Abell encountered 1 in 131 patients (0.7 per cent) and Behrend found only 1 (0.6 per cent) in 158 cases of cancer of the colon and rectum.

Sex incidence and cancer site. Multiple carcinomas occurred more than twice as often in men as in women. There were 11 cases in the male as compared with 5 in the female sex. This ratio may in part be due to the fact that cancer in the large bowel is more frequently met in men. Railford, Heydemann, and others have reported a 2:1 preponderance in single cancer in the male sex. The experience at our hospital does not corroborate these findings. In 344 patients, there were 185 men with cancer in the large intestine as compared

TABLE III.—DOUBLE CARCINOMAS OF THE LARGE INTESTINE—COLLECTED FROM THE LITERATURE (1933–1943)

Author	Reported	Sex	Age	Location	Location
Abell	1933	M	40	Cecum	Transverse
White	1933	M	37	Hepatic flexure	Sigmoid
Cokkinis	1934	F	66	Pelvic colon	Descending colon
		F	68	Pelvic colon	Transverse
		M	60	Pelvic colon	Transverse
Pfeiffer†	1935	M	—	Descending colon	Rectosigmoid
		—	—	Rectum	Sigmoid
		—	—	Rectum	Sigmoid
Lillienthal††	1935	—	—	Colon	Colon
Lewisohn††	1935	—	—	Colon	Colon
Thompson	1936	M	51	Pelvic colon	Pelvic colon
		M	54	Cecum	Transverse
		M	36	Transverse	Ascending colon
Burke	1936	M	50	Rectum	Hepatic flexure
Greenwood	1936	M	52	Rectum	Rectum
Kent and Sawyer	1937	F	59	Hepatic flexure	Transverse
Behrend	1937	—	—	Ascending colon	Rectosigmoid
Siebert	1937	F	58	Rectum	Sigmoid
		F	64	Pelvic colon	Transverse
Hortolomei	1937	F	54	Cecum	Transverse
Brindley	1938	M	39	Splenic flexure	Ascending colon
		M	43	Rectum	Transverse
		F	59	Rectum	Transverse
		M	71	Sigmoid	Sigmoid
		F	62	Descending colon	Rectum
		M	25	Rectum	Rectum
		M	35	Rectum	Rectum
		M	46	Rectum	Rectum
Gabriel	1938	F	37	Pelvic colon	Rectum
		M	73	Pelvic colon	Rectum
		M	68	Transverse	Rectum
		M	54	Transverse	Rectum
Graham‡‡‡	1939	—	—	Rectosigmoid	Sigmoid
		—	—	Rectosigmoid	Rectum
Bacon	1939	M	77	Rectosigmoid	Rectum
		M	83	Rectum	Rectum
		M	53	Rectum	Rectum
Torres	1939	M	48	Rectum	Rectum

TABLE III.—DOUBLE CARCINOMAS OF THE LARGE INTESTINE—COLLECTED FROM THE LITERATURE (1933–1943)—Continued

Author	Reported	Sex	Age	Location	Location
Schweiger and Bargen	1940	M	58	Sigmoid	Rectum
		M	54	Descending colon	Descending colon
		M	55	Rectum	Rectum
		F	43	Rectum	Rectum
		M	45	Descending colon	Rectum
		M	45	Rectum	Rectum
		M	70	Descending colon	Rectum
		M	59	Rectum	Rectum
		F	41	Sigmoid	Rectum
		F	50	Cecum	Ascending colon
		F	59	Ascending colon	Sigmoid
		F	59	Transverse	Cecum
		F	39	Rectosigmoid	Transverse
		F	48	Rectum	Sigmoid
		M	55	Sigmoid	Rectum
		M	78	Cecum	Sigmoid
		M	55	Cecum	Rectum
		M	65	Ascending colon	Rectum
		M	40	Descending colon	Cecum
		F	65	Rectum	Cecum
Gregg and Dixon	1941	M	53	Transverse	Transverse
De Amnesti	1941	F	52	Rectum	Sigmoid
Tullis	1942	M	40	Rectum	Transverse
		M	58	Rectum	Rectum
Herrlin and Mersheimer	1943	M	71	Ascending colon	Sigmoid
Hellendall	1943	—	—	Splenic flexure	Descending colon
		—	—	Colon	Cecum

† In discussion of paper by Klingenstein
†† Quoted by Klingenstein
‡‡‡ Quoted by Bacon

with 159 in women, a ratio of about 5:4 (Table I).

Age incidence. The youngest patient was 28 and the oldest 71 years. One of the 3 cases with three carcinomas was 36 years of age. Eight were over 65 years and 14 of the patients over 50 years (Table V). The average age for cancer occurring as a single lesion in 344 pa-

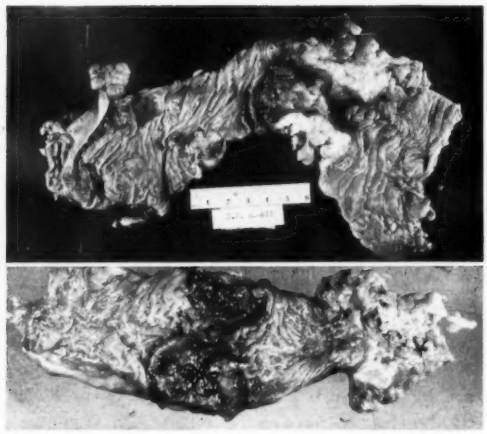


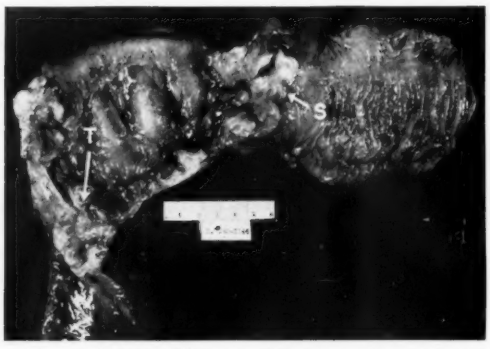
Fig. 1. Case 10. Two metachronous carcinomas in the large intestine. Above, splenic flexure; below, rectum.

tients was found to be 56.1 years. Multiple carcinomas in the large intestine occurred at an earlier age. Thus in the combined series (Table II), the average age for 2 malignant growths was 54.8 years and for 3 or more cancers, 51.9 years.

Multiple cancers and polyps. Lockhart-Mummery, Warren, and Dukes have long emphasized the importance of considering polyps in the intestine as precancerous. Once a malignant change has occurred in a previously benign adenoma, difficulty may arise in identifying the cancer as having arisen in a simple polyp. These investigators have shown conclusively that such a change does occur more frequently than we suspect. The relationship between multiple carcinomas and the presence of polyps led to an investigation of 84 consecutive necropsies on patients known to have died as a result of cancer of the large intestine. In 21 (25 per cent) one or more polyps were present. These were more frequent in colon carcinoma than in rectal malignant lesions. In patients with cancer in the rectum, only 1 in 20 (5 per cent) had an accompanying polyp. Of the 16 cases with multiple cancers in the colon and rectum, 6 (37.5 per cent) had polyps in addition to the malignant lesion. In 4 of these the polyp proved to be cancerous on microscopy. One patient (Case 10) was known to have had a benign polyp in the rectum at a time a splenic flexure cancer was removed. One year later he returned with an extensive infiltrating carcinoma in the place of the previously benign growth.

CASE REPORTS

CASE 1. M.S., a 45 year old white female, was first admitted in September, 1924, because of abdominal pain, obstipation, and loss of weight. Operation revealed an annular carcinoma of the transverse colon near the hepatic flexure. An exteriorization of the bowel was done followed by closure of the colostomy. She returned in 1934 with the same complaints. At exploration no evidence was present of a recurrence at the anastomosis, but the site was narrowed by scar tissue. In the belief that this pathology was the cause of her complaints, the bowel was opened longitudin-



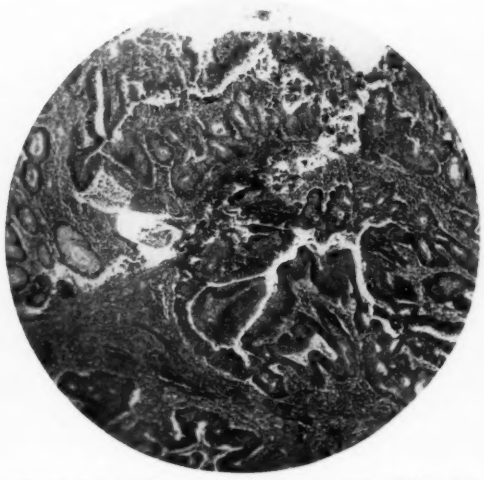


Fig. 2. Case 13. Three synchronous carcinomas in the colon. a, left, two present in one specimen, in the transverse colon *T* and in the splenic flexure, *S;* b, right, photomicrograph of third carcinoma in the descending colon.

ally and closed in the transverse axis. She reacted poorly from this procedure and died a few days later. At autopsy an unsuspected fungating carcinoma was found in the transverse colon near the splenic flexure.

CASE. 2. M.M., a white male, 59 years of age, was admitted in June, 1935, with epigastric pain, nausea, vomiting, and anemia. He stated that 2 years previously he was operated upon for "tumor," but no resection was done. He then had a series of "cancer serum" injections followed by x-ray therapy. On examination he presented a markedly cachectic and wasted appearance. There were 2 large masses in his abdomen, one in the epigastrium and the other in the right iliac fossa. He died soon after admission. Necropsy revealed the presence of distinct cancers. The one was in the cecum and the second, in the transverse colon, had penetrated the stomach producing a gastrocolic fistula.

CASE 3. G.G., a 28 year old white female, was admitted in November, 1935, with advanced intestinal obstruction and died 36 hours later. Autopsy uncovered both a constricting carcinoma of the sigmoid and an ulcerating malignant lesion 8 centimeters distal to the first lesion.

CASE 4. J.L., a 65 year old white man, was admitted in June, 1938, because of vomiting, abdominal pain, and weight loss. A cecostomy was done because of marked distention. Ten days later, at operation, 2 malignant lesions, one in the splenic flexure and the other in the descending colon, were noted. A Rankin obstructive resection was performed.

CASE 5. A.G., a 57 year old white male, had a Rankin resection done in June, 1939, for a carcinoma of the descending colon. Several months later he was admitted with intestinal obstruction. Operation showed a carcinoma of the transverse colon.

CASE 6. P.L., female, white, 51 years old, was admitted in June, 1939, with intestinal obstruction thought to be caused by adhesions secondary to a cholecystectomy (1924). Exploratory operation revealed an annular carcinoma of the transverse colon.

Fig. 3. Case 15. Three synchronous carcinomas of colon and rectum. a, left, One cancer at *C* in cecum and a second at *T* in the transverse colon; b, right, photomicrograph of a third carcinoma occurring in the rectum.

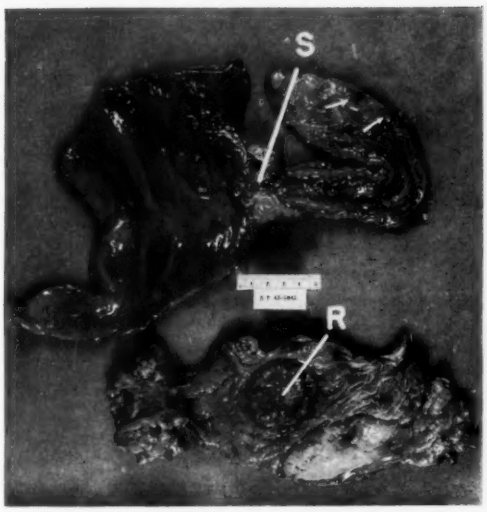


Fig. 4. Case 16. Two synchronous carcinomas. *S*, splenic flexure; *R*, rectum.

Following a cecostomy she developed pneumonia, and resection had to be delayed. After 7 weeks the lesion was removed and a primary anastomosis was done. Four months later, a follow-up investigation by means of a barium enema revealed a filling defect in the descending colon. Laparotomy confirmed the diagnosis of carcinoma.

CASE 7. D.B., a 62 year old white male, was seen in January, 1939, with intestinal obstruction. Re-

moval of the involved bowel was done, and the examination of the specimen showed two carcinomas 3 centimeters apart in the descending colon.

CASE 8. S.L., a white male, 71 years old, was admitted for the second time in November, 1939. His first admission was in 1928 for a carcinoma of the sigmoid. This had been removed. After 11 years he was readmitted with acute intestinal obstruction caused by a constricting malignant growth of the hepatic flexure.

CASE 9. I.S., a 70 year old man, was admitted in December, 1941, because of diarrhea, weight loss, and abdominal pain. Operation showed the cause to be a cancer of the descending colon. A wide excision was performed. Examination of the specimen revealed two malignant growths 9 centimeters apart.

CASE 10. D.G., a 65 year old male, was first seen in February, 1941, because of abdominal cramps, distention, and obstipation. Sigmoidoscopy revealed a mass, and biopsy proved tissue removed to be benign. A barium clysma and contrast study showed a filling defect in the splenic flexure, and at operation a carcinoma in this area was removed. One year later he returned with rectal bleeding and constipation. Examination of the rectum disclosed a large mass completely encircling the wall and filling the lumen. This tumor proved to be malignant and was removed by a one stage abdominoperineal resection.

CASE 11. L.H., a white male, 68 years of age, was admitted in June, 1943, with acute intestinal obstruction. A scout film revealed distention from the hepatic flexure to the descending colon. A palliative colostomy was performed, but due to renal and pulmonary complications, the patient died. Necropsy revealed an annular carcinoma of the splenic flexure and an unsuspected malignant lesion in the ascending colon.

CASE 12. H.D., 64 year old white female, had had a resection of the transverse colon for cancer in 1935. She was well until November, 1943, at which time she began to vomit and had increasing difficulty at stool.. Roentgen-ray study disclosed a splenic flexure lesion. This proved to be malignant and was removed by an obstructive resection.

CASE 13. B.P., a 68 year old man, was admitted in June, 1942, with distention and pain. Barium studies had disclosed an obstruction at the splenic flexure. At operation 2 lesions were discovered, 1 in the transverse colon and a second in the splenic flexure. A wide resection was performed, with removal of the descending colon, the splenic flexure, and half of the transverse colon. Examination of the specimen later revealed an unsuspected third tumor in the lower descending colon. This was a polyp that had undergone malignant change.

CASE 14. C.B., a 54 year old white female, had undergone a resection for sigmoid carcinoma, at another institution in May, 1941. Her convalescence was poor, and when seen by one of us (H.L.B.) in January, 1942, she presented a marked anemia and general weakness. On rectal investigation, a mass was palpated about 8 centimeters from the anal orifice, and a larger tumor was felt beneath the liver. Biopsy proved the first neoplasm to be malignant and a barium enema disclosed a second obstructive lesion in the hepatic flexure. An exteriorization of the right colon with a double barreled colostomy was performed in April, 1942. Her course was stormy and further surgery at this time was out of question. When she was re-examined several months later the rectal mass was fixed and considered to be nonresectable. She was given a long course of deep therapy. Two years later, because of her marked improvement both generally and locally, an exploratory operation was performed (February, 1944). The rectum and tumor were found to be resectable, and there was complete absence of any metastatic spread. The histopathology was that of a colloid adenocarcinoma similar to that in the other two locations.

CASE 15. L.R., a 36 year old white male, was admitted on November 20, 1939. Eight months previously, because of diarrhea, he was sigmoidoscoped, but no lesion was found. He improved with diet and later returned for re-examination. Sigmoidoscopy at this time showed a carcinoma of the rectum. Abdominal palpation disclosed the presence of a tumor in the right lower quadrant. Exploration confirmed the impression that a second cancer was present in the cecum and also uncovered a third carcinoma in the transverse colon. A hemicolectomy was performed, the cecal and colon cancers being removed, followed in 3 weeks by a one stage abdominoperineal resection for carcinoma of the rectum.

CASE 16. A 63 year old white male was admitted in August, 1943, because of abdominal cramps and distention. He had had rectal bleeding for 6 months and had lost 20 pounds in weight. Rectal palpation disclosed a malignant ulcer on the right lateral wall about 8 centimeters from the anus. This did not explain the obstructive symptoms, and the possibility of a second cancer in the colon was considered. At operation an annular carcinoma in the splenic flexure as well as the rectal lesion was noted. A left colectomy and abdominoperineal resection were performed.

In Cases 1, 5, 8, 10, and 12 the second lesion occurred metachronously after intervals of 10, 1½, 11, 1 and 7½ years, respectively. In the last 3, the diagnosis was made and resection was performed. Cases 2, 3, and 11 were late admissions and the multiple cancers were found at the postmortem examination. Fenger, in 1888, reported a case in which he did a colostomy proximal to a sigmoid neoplasm. His patient died without any relief from the intestinal obstruction. Autopsy disclosed the presence of a second cancer proximal to the colostomy. In Case 11 patient had a similar experience in that a palliative colostomy was done between 2 cancerous growths. Failure, in Cases 6 and 14, to recognize the presence of

TABLE IV.—THREE CARCINOMAS OF THE LARGE INTESTINE—COLLECTED FROM THE LITERATURE (1933–1943)

Author	Reported	Sex	Age	Location
Cokkinis	1934	M	64	Pelvic colon, iliac colon and descending colon
Klingenstein	1935	F	43	Transverse, sigmoid and ascending colon
Schweiger and Bargen	1940	F	44	Transverse, cecum, and ascending colon
		M	49	Cecum, sigmoid and descending colon
		F	56	Sigmoid, three lesions
Hellendall	1943	—	—	Cecum, rectum and splenic flexure

TABLE V.—MULTIPLE CARCINOMAS OF THE LARGE INTESTINE—JEWISH HOSPITAL (1934–1943)

Case	Hospital	Sex	Age	Location
1	170176	F	55	Transverse colon, 2 lesions
2	181519	M	59	Cecum and transverse colon
3	185185	F	28	Sigmoid, 2 lesions
4	212845	M	65	Splenic flexure and descending colon
5	218484	M	57	Descending colon and transverse colon
6	222694	F	51	Transverse and pelvic colon
7	218857	M	65	Descending colon, 2 lesions
8	228900	M	71	Sigmoid and hepatic flexure
9	249847	M	70	Descending colon and sigmoid
10	240519	M	65	Splenic flexion and rectum
11	266522	M	68	Ascending colon and splenic flexure
12	270001	F	65	Transverse colon and splenic flexure
13	254609	M	68	Transverse descending colon, and splenic flexure
14	252840	F	54	Sigmoid, hepatic flexure, and rectum
15	220064	M	36	Cecum, transverse colon, and rectum
16	267753	M	63	Splenic flexure and rectum

a second cancer resulted in loss of precious time. The poor results obtained following the removal of one cancer were attributed to metastatic spread when in reality the failure to improve was due to the presence of a second lesion that had been overlooked. In contrast to these are Cases 4, 13, 14, 15, and 16, in which careful investigation and exploration revealed the presence of more than one tumor, and the operations were planned accordingly.

The practice of wide excision of intestine with several inches, if possible, of apparently normal bowel proved of value in Cases 7, 9, and 13. In each of these an unsuspected malignant lesion was found in the resected tissue several centimeters away from the cancer for which the operation was being done. In Case 10, a rectal polyp diagnosed as benign was ignored because a splenic flexure carcinoma was discovered. One year later this polyp had become an extensive infiltrating carcinoma of the rectum necessitating a major resection and a permanent colostomy.

Case 14 is interesting in that a sigmoid carcinoma was removed in 1941, a hepatic flexure cancer in 1942, and a rectal cancer known to be present in 1942 was not removed until 1944. Examination of the liver, the mesentery, the preaortic region, revealed no evidences of metastases. She subsequently came to necropsy after a bronchopneumonia at which time final proof was offered of the absence of any metastatic spread.

Case 15 is worthy of special mention because of the occurrence simultaneously in a 36 year old man of 3 cancers, located in different segments of the large intestine and the successful removal of all. Mayo, Klingenstein, Bargen and Rankin, and Schweiger and Bargen have reported comparable cases, but in none of these did the malignant growths occur synchronously. Norbury recorded a similar case occurring in a man of 76 years. The lesions were in the rectum, the transverse colon, and the sigmoid.

OBSERVATIONS

Polyps and multiple cancers. The frequency with which polyps and adenomas appear in the large intestine and their relation to the formation of multiple cancers must enter into any discussion of this subject. We are not concerned here with the familial congenital adenomatosis or generalized polyposis of the colon. That this is a true Mendelian dominant has been pointed out by Lockhart-Mummery. The frequency of cancerous changes in this disease is generally accepted to be at least 40 per cent, and Fitzgibbon and Rankin claim malignant change to be as high as 85 per cent. However, the presence of one or more benign polyps in the colon and rectum is not a rare

finding in patients not considered to have familial polyposis. The large intestine is a common site for the formation of polyps, which according to Lawrence occur 12 times as frequently in the large as in the small intestine. Undoubtedly, many carcinomas in the large bowel arise from pre-existing adenomas, but there is no evidence to support the belief that all malignant growths in this area arise from this source.

Mayo found that polyps were present in 34 per cent of patients with cancer and that 14 per cent of these were already malignant. In contrast to this, he found that in noncancerous patients polyps were found in only 16 per cent and 8 per cent of these had undergone malignant change. According to Hardy, 40 per cent of all carcinomas of the large intestine start as benign polyps.

Our findings are almost similar and show a marked tendency to cancerous change in intestinal polyps in known cancer patients. Six of our multiple carcinoma cases (37.5 per cent) had polyps and in 67 per cent of these malignant transformation had occurred. How many of the remaining patients had cancer that arose in previously benign polyps could not be determined because the lesions were too extensive at the time the lesions were examined. It is conceivable that if cancer of the large intestine can arise in one area, the tendency or susceptibility toward cancer can influence a similar transformation in a simple polyp. We cannot agree that all cancers in this region originate in previously benign polyps in view of our finding that polyps were present in only 25 per cent of our cancer cases and in only 5 per cent of rectal carcinomas. However, the chances for a benign polyp to undergo malignant change in a patient known to have cancer in some other part of the large intestine or who belongs to a cancer family is great. These polyps should be attacked early and vigorously and not be allowed to grow. Our experience does not corroborate the statement by Boyd that "once malignancy occurs in one of these adenomata the others tend to disappear."

Clinically and experimentally the evidence has accumulated against the belief that one cancer can bestow on the patient any degree of immunity against the appearance of a second, or even third, cancer. Generally accepted now is the belief that malignant growths result from the action of an extrinsic force capable of causing abnormal cell growth on a susceptible intrinsic factor. Once a cancerous tumor has been removed from a patient, that individual should be suspect to the end of his days. He should be observed for evidences of other primary malignant neoplasms in the colon and rectum. Any polyp, even if symptomless, should be removed early and not when the patient has a change in bowel habit, rectal bleeding, and other evidences of malignant change. Whatever the susceptibility factor may be, it is evident that the carcinogenic tendency is sufficiently strong to produce multiple cancers in certain people as easily as it produces single lesions in others.

Longevity in multiple cancers. The conclusion drawn by Hanlon and by Orr, that patients with multiple cancers are older than those with single lesions is not confirmed by this study of multiple carcinomas limited to the large intestine. Hanlon claimed that because of earlier diagnosis and treatment, the survival period permitted the development of a second cancer. This in part may be true in malignant lesions occurring at different time intervals, but does not satisfactorily explain multiple cancers occurring synchronously. Warren and Gates, basing their study on a large series of cases including those reported by Hanlon, found the age to be no different for single than for multiple carcinomas.

Double lesions in the large intestine as we found them in the collected series combined with our own occurred 1.3 years earlier than our single cancers. Patients with three malignant neoplasms were 4.2 years younger than those with only one tumor. These findings contradict the belief that multiple carcinomas develop only on the basis of longevity.

Multiple cancers versus metastases. Skepticism might be entertained that multiple lesions are not primary new-growths, but that one is a metastasis from the other. The problem of proving multiple primary cancers as they occur in the large intestine based on histopathology may at times be difficult in view of the fact that they arise from similar epithelial cells. When there is a difference in the histology

there can be no doubt of the authenticity of the case. But when the microscopic appearance is the same, such genuineness cannot be easily established. The possibilities of fragments of cancer tissue breaking off the primary growth and becoming implanted on the mucous membrane at some other site must indeed be small. The passage of feces and mucus propelled by the constant peristaltic action would strongly influence the chances of any malignant cells clinging to the mucosa long enough to become a transplant. Certainly the chances are even less in those cases in which the older lesion is in the distal part of the bowel and the younger tumor tissue is more proximally located. One cannot claim metastatic origin of a double cancer if, after removal of a second growth, the patient should remain well and free from any evidences of the existence of metastases. Case 14 of our series offered incontrovertible testimony that similarity of the histopathology may occur, and the multiple cancers can be primary tumors. Her three carcinomas were colloid adenocarcinoma indistinguishable from each other. Located in the sigmoid, in the hepatic flexure, and in the rectum, successively removed in 1941, 1942 and 1944, no evidence at the time of the last operation was found of any metastatic spread. Final proof of the absence of metastases was offered at necropsy.

SUMMARY

1. The presence of a carcinoma does not confer immunity against the appearance of other primary cancers in the large intestine.

2. A predisposition or susceptibility to cancer is more important in the production of multiple carcinomas than chance, age, or sex.

3. Sixty-six cases of double and 6 patients with 3 cancers were collected from the literature since 1932. To these are added 13 patients with 2 cancers and 3 patients with three malignant growths.

4. Polyps were present in 25 per cent of single cancer patients and in 37.5 per cent of those with multiple carcinomas. In 67 per cent of the latter group, malignant degeneration had taken place.

5. The frequency of multiple cancers in our series was found to be 4.6 per cent.

6. There were 11 cases in men and 5 in women.

CONCLUSION

Multiple cancers can occur in the large intestine either synchronously or metachronously and the importance of keeping this in mind is apparent. The prognosis in cancer resections is influenced by the presence of a second malignant lesion in that if overlooked death of the patient may ensue because of the continued growth of the lesion.

Any patient who has had one carcinoma removed should be observed carefully and repeatedly for the possible development of a second new-growth. The use of the proctoscope, sigmoidoscope, and contrast barium enema should be resorted to in every examination of the colon and rectum. The presence of a rectal carcinoma should be a signal to continue the investigation of the colon. The discovery of a colon lesion by roentgen-ray or by palpation should be followed in every case by direct visualization of the lower intestine. Finally, at operation a careful exploration of the entire bowel should be made. Unquestionably many "poor results" in the treatment of cancer of the large intestine can be attributed to the fact that a second lesion was missed. Brindley very aptly stated, " a patient with one cancer is a good subject for the development of a second, and is more susceptible than one who is cancer free."

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FURTHER STUDIES ON THE PREPARATION AND USE OF SULFATHIAZOLE OINTMENT IN THE TREATMENT OF BURNS

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THE use of sulfathiazole ointment in the treatment of burns has been previously reported by Allen, Owens, Evans, and Dragstedt (4). The purpose of this report is to describe further observations on the preparation and use of several kinds of sulfathiazole ointment and to present an evaluation of these from the standpoint of emulsification properties, stability, effect on the healing of tissues, sulfathiazole diffusion, and bacteriostatic properties.

The general recent trend in local burn therapy has been to utilize some sort of grease dressing in view of the accumulating evidence that the tannic acid treatment of burns has a number of undesirable features, such as contributing to liver necrosis (26), and delaying epithelial regeneration (8).

An ordinary petrolatum or vaseline dressing is probably the most widely used local treatment for burns at the present time due in large measure to the excellent results reported by Allen and Koch (3) and by Siler and Reid (21). For burns which can be cleansed and treated soon after the burn occurs the petrolatum dressing appears to be quite a satisfactory method, especially when fine mesh gauze and pressure dressings of mechanics' waste are used. However, if the burned area has an opportunity to become contaminated and considerable delay is encountered before final treatment is instituted, it is possible for severe infection to develop. This may not only delay healing but may also destroy viable nests of epithelium in the burned area which would otherwise offer a nucleus for regeneration of an epithelial surface. It is especially for such cases in which cleansing procedures are not feasible and in which contamination or beginning infection has occurred that there is a place for a bacterial inhibiting agent in whatever grease dressing is utilized for local therapy. It is possible to obtain an effective inhibition of bacterial growth in burned areas by the use of sulfonamides administered systemically as was reported in the symposium on the management of the Cocoanut Grove burns at the Massachusetts General Hospital by Cope, Lyons, Cannon. However, this requires the maintenance of a therapeutic blood level, which presents certain hazards and problems in the care of many severely burned patients, especially when adequate laboratory facilities are not available.

To obtain appreciable diffusion of sulfathiazole from a petrolatum base, it is necessary to add some type of surface active agents to the ointment base. This surface active agent may permit the emulsification of petrolatum with water, thereby permitting the sulfathiazole to be liberated from the aqueous phase of the emulsion. Or, as we have found, the surface active agent may permit the liberation of sulfathiazole from the petrolatum without emulsification. There are a great many surface active agents which are recently available (25) and their special properties lend themselves to uses in many ways not only in therapeutics but also in various commercial industries, such as in cosmetics, paints, insecticides, and so forth. The emulsification and sulfathiazole diffusion properties of such proprietary ointment bases as aquaphor or hydrosorb, which are for the most part composed of petrolatum, are due to the presence of certain surface ac-

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tive agents added to the petrolatum. These proprietary bases have been studied and in addition ointments have been made up with petrolatum to which varying concentrations of known surface active agents were added.

The surface active agents which have been studied particularly have been the Atlas spans and tweens (5). This represents a group of mannitol and sorbitol derivatives (22) which vary in their physical properties from thin liquids to viscous oils or waxes. These materials, which are nonelectrolytes, vary from complete oil solubility to complete water solubility. The spans are predominately oil soluble and water insoluble, although they are dispersible in water. The tweens are for the most part soluble in water. Each of these surface active agents have properties which lend themselves to particular uses. Of these agents, the most satisfactory for obtaining a stable petrolatum water emulsion was found to be arlacel C, which is a purified form of span 80, and is essentially sorbitan monooleate.

The spans and tweens are miscible with each other and in some instances may be combined to obtain a particular surface action phenomenon not possessed by either separately. For example, it was found that when tween 80 was added to the aqueous phase of a petrolatum water emulsion, the diffusion of sulfathiazole from such an emulsion was appreciably greater than when only arlacel C was used for producing the emulsion. Furthermore, it expedites the liberation of sulfathiazole from petrolatum even when the petrolatum has not been emulsified with water. Tween 80, which is a polyoxyalkylene ether of a partial oleic acid ester, was also found to increase slightly the solubility of sulfathiazole in aqueous solution and to increase the extent to which sulfathiazole powder could be suspended in water. Another feature of the tween 80 was its detergent properties which are applicable in the cleansing of wounds contaminated by oils or greases where one would not choose to use an irritant solvent.

Two general classes of sulfathiazole ointments were studied. The nonemulsion ointments were prepared by adding sulfathiazole to a proprietary petrolatum base, such as hydrosorb or aquaphor, or to petrolatum which contained spans or tweens or both. The emulsion ointments were prepared by adding sulfathiazole in water to these grease bases. The method of preparing the ointments is complicated by the fact that heat sterilization of these materials after mixing results in the sulfathiazole caking or settling out in the grease base or separation of the emulsion. In view of the bacterial contaminations found in sulfonamide ointments by Fisher the ointments which were designed for clinical use were prepared in the operating room from ingredients which had been subjected to heat sterilization and then mixed under sterile precautions, with the aid of a manual or electric mixer.

A laboratory test was devised for evaluating the diffusion of the sulfathiazole from the various ointment preparations. This was carried out by suspending 10 grams of ointment in a fine mesh gauze bag in a jar containing 100 cubic centimeters of water. The determinations of the sulfathiazole content of the water were made after varying periods, changing the water from time to time to ascertain the extent to which the diffusion was maintained. The results of this are presented in Table I.

These observations demonstrate that certain surface active agents expedite the diffusion of sulfathiazole from a petrolatum base into a surrounding aqueous medium. In the nonemulsion ointment series, there were some instances in which proprietary bases did not liberate sulfathiazole much better than petrolatum alone. In other instances there was an appreciable liberation of sulfathiazole which was most marked in the first 24 hours, although subsequent liberation was somewhat reduced. The concentration of sulfathiazole in the ointment base did not appear to make much difference in the rate and amount of sulfathiazole diffusion in most instances. The emulsion ointment preparations demonstrated better original diffusion and continued diffusion than the nonemulsion ointments. The ointment which appeared to have the most satisfactory stability and diffusion properties was the one prepared from petrolatum with arlacel C in the oil phase and tween 80 in the aqueous phase with sulfathiazole (Formula).

FORMULA

Oil phase	
Petrolatum	48 c.c.
Arlacel C	2 c.c.
Aqueous phase	
Sulfathiazole	5 gm.
Tween 80	¼ c.c.
Water q.sa. d	100 c.c.

One of the methods of evaluating the various ointment preparations was to apply these to the raw surface of a dermatone graft donor area and observe the effect on healing such as was described by Cannon and Cope (8). These tests showed that the sulfathiazole ointments did not appreciably retard healing as compared with petrolatum. In a few instances there was some delay in epithelization as compared with petrolatum, although in many instances the sulfathiazole ointment appeared to contribute to a more rapid rate of healing than was observed for petrolatum. Tannic acid was found to delay epithelization when compared with petrolatum as was pointed out by Cannon and Cope. Evidence of maceration of the tissues was less frequently observed with the emulsion type of ointment than with the nonemulsion ointments.

In regard to the observations made subsequent to healing it was found that a considerable proportion of the donor areas treated with sulfathiazole in aquaphor developed keloids. This was also observed with other sulfathiazole preparations from time to time. However, there was distinctly less tendency for the emulsion ointments to be associated with keloid formation than the nonemulsion type. Tannic acid did not lead to keloid formation in any of the donor areas in our series. Petrolatum was seldom associated with keloid formation. Sulfathiazole crystals applied to donor areas which were then covered with petrolatum did not appear to be associated with keloid formation except in one instance. The emulsion ointments containing arlacel C and tween 80 appeared to be associated with keloid formation less frequently than the emulsion ointments prepared from proprietary "absorption" bases.

One instance of sensitivity to sulfathiazole was observed when 1 gram of sulfathiazole crystals was applied to part of a dermatone donor area. This patient had been given sulfathiazole by mouth about 8 months previously and he had developed evidence of sensitivity at that time. The donor area exhibited a marked local sensitivity reaction consisting of itching and burning and a continual bleeding from this area which lasted several days even though the sulfathiazole was removed in the first 24 hours. There was definite delay in epithelization in this area, as compared with the area which was covered originally with petrolatum alone. In addition, the patient exhibited a generalized sensitivity reaction consisting of itching, urticaria, and erythema.

Sulfathiazole ointment has been used in the treatment of 60 cases of burns at the University of Chicago Clinics. The ointment preparations which were used consisted of 5 per cent or 20 per cent sulfathiazole in aquaphor, 5 per cent sulfathiazole in aquaphor-water emulsion, and 5 per cent sulfathiazole in petrolatum-water emulsion (water in oil type of emulsion with arlacel C and tween 80 as surface active agents).

The preliminary treatment which was carried out with rigid aseptic precautions consisted of gentle cleansing of the burned surface with soap and water and copious irrigations with physiological saline solution. Débridement of easily detachable skin was done and usually the blisters were opened. Adequate sedation was obtained with morphine and it was not found necessary to use general anesthesia on any of these cases. Cultures of the burned area were usually taken before and after the cleansing procedure. Photographs were taken in most of the cases before the treatment was started.

The ointment was spread on fine mesh gauze (40 by 44) and applied to the burned area. Large amounts of mechanics' waste were spread over the gauze and wrapped securely with bandages to obtain the desired pressure effect on the burned area. Additional compression was obtained in some cases by the use of elastic bandages on the extremities or elastoplast adhesive on the trunk. A rather important point which has been consistently observed was the analgesic effect of the sulfathiazole ointment. This has made it possible to minimize sedation to a considerable extent as this analgesic action is usually noticed im-

TABLE I.—DIFFUSION OF SULFATHIAZOLE FROM 10 GRAMS OF OINTMENT INTO 100 C.C. OF WATER AT 37° C. IN MILLIGRAMS

	0–1 Day[1]	1–2 Days	1–3 Days[1]	3–5 Days[1]	5–13 Days
Petrolatum base (without water) Petrolatum with 5 per cent sulfathiazole	1.2	Trace	.7	Trace	Trace
Amerchol with 5 per cent sulfathiazole	0	Trace	.5	.8	1.
Aquaphor with 5 per cent sulfathiazole	1.3	.7	1.1	.8	1.4
Aquaphor with 20 per cent sulfathiazole	.6	Trace	1.0	Trace	1.77
Hydrosorb with 5 per cent sulfathiazole	.7	Trace	.5	Trace	.83
Petrolatum with 5 per cent sulfathiazole, 1 per cent tween 80	3.3	.8	1.0	Trace	Trace
Petrolatum with 5 per cent sulfathiazole, 2½ per cent tween 80	3.8	1.0	1.8	Trace	1.1
Petrolatum-lanolin 5 per cent sulfathiazole	1.0	Trace	.6	Trace	Trace
Petrolatum-lanolin 20 per cent sulfathiazole	3.2	1.1	3.6	1.0	1.4
Petrolatum-water emulsion (50 per cent water) Amerchol with 5 per cent sulfathiazole	2.7	.8	1.6	1.2	3.2
Aquaphor with 5 per cent sulfathiazole	2.5	1.3	4.7	2.3	5.4
Hydrosorb with 5 per cent sulfathiazole	3.3	1.3	5.3	2.2	5.
Petrolatum with 2 per cent arlacel C & 5 per cent sulfathiazole, ¼ per cent tween 80	3.9	3.4	9.6	6.	13.5

[1] Indicates change of water to determine continued diffusion of the sulfathiazole from the ointment.

mediately after the application of the ointment.

Blood counts and cell volume determinations were made in the more severe burn cases and plasma was administered as needed. It was of interest to note that in one patient who was treated within 20 minutes after the burn occurred there was a hemocentration of 12 per cent during the course of the cleansing and dressing procedure which required about 30 minutes. This point will be discussed in relation to the effectiveness of the pressure dressings in preventing loss of plasma.

The original dressing applied to the burned area was generally left in place for 10 days to 2 weeks. When the dressing was removed at this length of time many of the burned areas were completely healed. If the healing was not complete the sulfathiazole ointment was reapplied and left on for another week. In this series of cases there was only one which was not substantially healed in 3 weeks and which required skin grafts. This does not include the original cases reported by Allen and associates, in which it was necessary to resort to skin grafts in 2 cases.

In the cases in which the emulsion type of ointment was used it was of interest to note that in many instances the skin surface was dry and free from evidence of maceration at the time of the removal of the dressing. Dry, scaly crusts were often adherent to the skin or to the dressing. When there were raw surfaces present there was very little exudate on the dressing in many of the cases. Cultures were usually taken after the removal of the dressings and photographs made.

In regard to the one case in this series which required skin grafts, the original dressings were removed on the eighth day at which time the burned skin of the leg appeared to be viable throughout and there was no evidence of infection. The leg was then treated with frequent changes of so called sterile saline dressings throughout that day and then fresh sulfathiazole ointment was reapplied that evening. When the dressings were changed again 1 week later there was obvious infection and necrosis of a considerable portion of the burned skin. It is probable that the infection was introduced during the course of the saline dressings. The bacteriostatic properties of the ointment were apparently not adequate to control the infection in this instance. The ointment used was the nonemulsion aquaphor preparation which was subsequently found to liberate less sulfathiazole than the emulsion type of sulfathiazole ointment.

The cultures taken before the cleansing procedure frequently demonstrated Staphylo-

Fig. 1. H. K., aged 21 years, burned right forearm by boiling water 3 days previously and originally treated by butesin pictate. Cultures of blister fluid showed Streptococcus viridans and Staphylococcus albus. a, left, Condition of forarm at time of admission. Cleansing with soap and water and débridement followed by irrigation was carried out (without general anesthesia). The raw surface was covered with 5 per cent sulfathiazole emulsion ointment (aquaphor 15 per cent, water 80 per cent) on fine mesh gauze. A pressure dressing was then applied. The dressing was left on for 12 days and then removed when there was complete healing except for few small raw surfaces. There was no evidence of exudate on the dressings and the skin was free from any evidence of maceration. Ointment was reapplied until 3 weeks after the burn when all raw surfaces were healed over. The blood sulfathiazole determinations showed only a trace of sulfathiazole, but the determinations on the urine showed 0.5 gram in the first 24 hours and from 5 to 10 milligram for the following week. b, right, Condition of forearm 29 days after the burn when healing has been complete for over a week. There are a few red areas but no evidence of residual keloid or contracture.

coccus aureus of the hemolytic type. In a number of cases Streptococcus hemolyticus was recovered from the burned area and in 1 case Streptococcus viridans. Staphylococcus albus was also a frequent contaminant. The cultures taken after the cleansing procedure were often sterile, but organisms found prior to cleansing were not infrequently present but less abundant in amount. Cultures taken after the original dressing was removed at 10 to 14 days were either sterile or demonstrated the presence of some of the organisms originally present. Some positive cultures were obtained after complete healing had occurred, and obviously were not of practical significance.

In general, it can be said that these burn cases represented what can be considered second degree burns judging from the excellent results which were usually obtained, except for the one case which developed infection. However, if a bacteriostatic agent had not been used on the burn cases which came in a day or more after the burn with positive cultures of pyogenic organisms, it is probable that infection would have developed in the burned skin in some instances. This would have destroyed the remaining viable epithelial elements and thus prevented spontaneous regeneration of an epithelial surface. These cases then would have been classified as third degree burns on the basis of the end-results.

A most interesting feature of this work on sulfathiazole ointments has been the use of surface active agents to obtain liberation of a water soluble medication from a petrolatum base. There are many instances in which it is desirable to have a grease base as a vehicle for a water soluble medicament, but unless some type of surface active agent is utilized, the medication may remain imprisoned and relatively inactive. Lanolin has some surface active properties and has been widely used as a vehicle for water soluble medications.

Proprietary "absorption bases" utilize the principle of incorporating surface active agents, such as diethanolamine oleate or cholesterol esters of oleic acid, in petrolatum. These commercial "absorption bases" are designed for a wide field of usefulness in the pharmaceutical and cosmetic trade and may not necessarily represent the most desirable concentration or selection of surface active agents for particular needs. In view of the results obtained with the sulfathiazole diffusion tests on "absorption bases" it would appear that improvements could be obtained in commercial bases designed primarily as vehicles for water soluble medications. The surface active agents which are most appropriate from the standpoint of obtaining good emolient properties in an ointment are not necessarily the most efficient for obtaining liberation of water soluble medications from petrolatum.

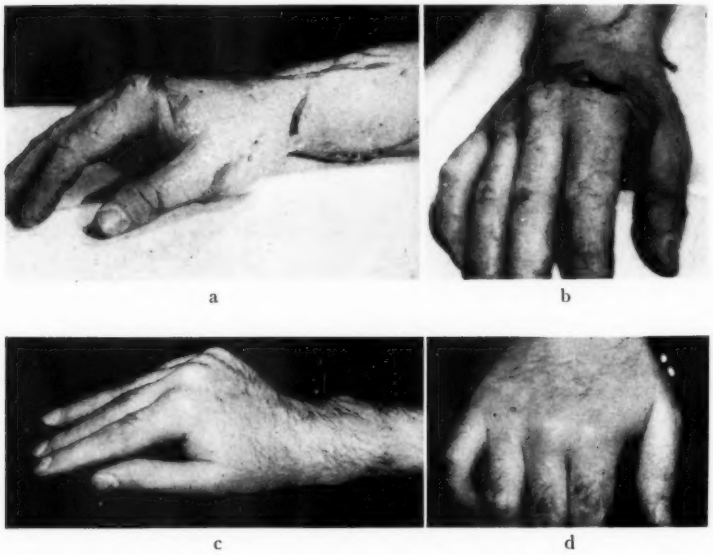
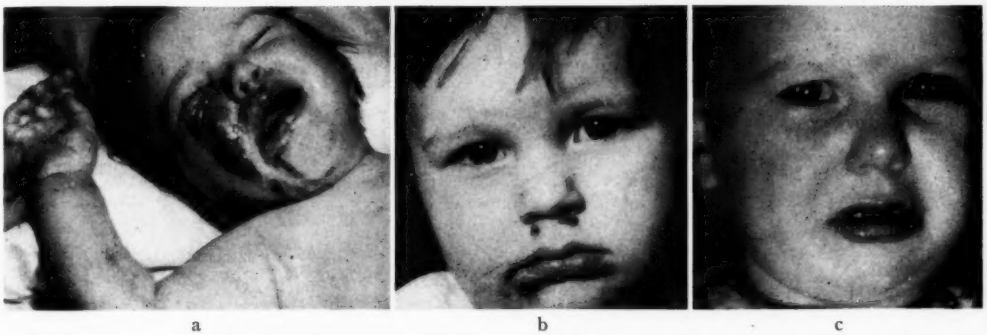


Fig. 2. J. G., aged 25 years, received burn of hand and wrist from benzene flame 20 minutes prior to admission. a, Condition of hand and wrist at time of admission immediately after burn. Cultures demonstrated Staphylococcus albus. b, Same. The hand and wrist were cleansed with soap and water. Débridement of separated skin was carried out. Irrigation with physiological saline solution, and application of 5 per cent sulfathiazole emulsion ointment (aquaphor 15 per cent, water 80 per cent) on fine mesh gauze was carried out. Then pressure dressings of mechanics' waste were put on. The dressings were left on for 12 days, at which time the hand was healed except for a few flaky crusts. Ointment dressing reapplied, and removed following week at which time hand was completely healed. c, Condition of hand at end of 7 weeks. There was no evidence of residual scarring or contracture. d, Same as c.

The fundamental mechanism of the action of these surface active agents appears to be primarily a matter of altering the opposing surface forces at the oil and water interface. These agents are mixed polar nonpolar molecules, which presumably exist as thin films, oriented at the surface or interface with their hydrophilic heads toward the aqueous phase and their hydrophobic chains away from it. By proper balancing of the hydrophobic hydrocarbon chain with hydrophilic groups the desired "clearance" or diffusion of the water soluble medication is obtained from the petrolatum base or the petrolatum-water emulsion.

In regard to the data on the cultures it was found that organisms could often be cultured from the burned area after the cleansing, débridement, and irrigation procedure. In most instances, however, the number of colonies which grew out was appreciably less as compared with cultures taken before the cleansing procedure. The evidence from the culture studies favors the view that these preliminary cleansing procedures are helpful in minimizing the magnitude of bacterial contamination in burned areas but not effective in completely eliminating it. There can be little doubt that cleansing, débridement, and irrigation have a place in the handling of burns as well as in other wounds wherever it is feasible to carry out such. It would be an unfortunate choice to omit these rather fundamental procedures in the treatment of wounds unless the facilities were not available to do so.

The demonstration of bacterial contamination in a burned area after relatively thorough cleansing, débridement, and irrigation lends support to the view that the local burn dressing should contain some bacteriostatic agent



a b c

Fig. 3. K. S., aged 18 months, suffered burn of face and elbow from hot grease one day previously at which time a tannic acid jelly was applied to face. a, Condition of face and elbow at time of admission. Cultures demonstrated abundant growth of Streptococcus hemolyticus and Staphylococcus aureus hemolyticus. Very gentle cleansing was done with soap and water followed by irrigation with physiological saline solution and then application of 5 per cent sulfathiazole emulsion ointment (aquaphor 15 per cent, water 80 per cent). Physiological saline dressings applied alternately for first 2 days to hasten removal of tanned crusted areas. b, Face 12 days after burn. Healing has occurred except for small crusted areas which healed over within the next 5 days. c, Condition of face 48 days after burn. There is no residual redness or scar visible at this time.

to deal with any residual contamination. If no cleansing procedures are used there is even greater need for a bacteriostatic agent. In cases in which considerable delay has occurred before the burn has had treatment and some degree of infection has already developed, there is again even more urgent need for some agent which could minimize or prevent further development of infection in the burned area. Petrolatum does not possess any inherent bacteriostatic properties. Its main virtue is that it is relatively inert and permits healing to progress under its protective cover unless the residual epithelial elements have been destroyed by the burn or by the development of infection.

To meet the need for a bacteriostatic agent in the local treatment of burns, the use of sulfathiazole in a petrolatum base which permits the diffusion of the sulfathiazole offers a reasonable means of minimizing or controlling the development of infection in the burned area. In view of the excellent results which were obtained with petrolatum alone by Allen and Koch and Siler and Reid it would appear desirable to continue to utilize petrolatum as the principal protective covering material on burned areas. The desired diffusion of sulfathiazole from the petrolatum can then be obtained by the use of the appropriate surface active agents.

It is appreciated that there is as yet no general agreement regarding the value of the local application of chemotherapeutic agents in the prevention and treatment of wound infections (20). The efficacy of the sulfonamides in the treatment of many infections, such as pneumonia and gonorrhea, however, may be regarded as definitely established. In these cases a factor in the success seems to be the production of a bacteriostatic concentration of the drug in the body fluids in contact with the invading parasite. In wounds the contaminating organisms are frequently sequestered or protected by their incorporation in coagulated protein exudates, necrotic tissue. or foreign bodies. Many of these organisms are susceptible to the bacteriostatic action of the sulfonamides, and these drugs have apparently very little effect on the growth of body cells. These facts present a challenge to the surgeon to control the various unfavorable factors in wounds so that he can secure for his patients the beneficient features of modern chemotherapy now enjoyed by his medical colleague. As emphasized by Whipple much can be accomplished in this direction by good surgery and for this there is no substitute. Of all types of wounds, it has appeared to us that burns present those features most favorable for the local use of chemotherapeutic agents. Foreign bodies are usually absent, surface

a b c

Fig. 4. M. G., aged 3½ years, suffered a hot water burn 1 day previously. a, Burn of back and elbow. Cultures demonstrated Streptococcus hemolyticus and Staphylococcus aureus hemolyticus. Cleansing and débridement (without general anesthesia) and application of 5 per cent sulfathiazole emulsion ointment (petrolatum 48 per cent, arlacel C 2 per cent, water 45 per cent, tween 80 ¼ per cent.) b, Back and elbow 19 days after burn. Approximately three-fourths of burned area has healed. c, Condition of back at 5 weeks; complete healing for several days.

contamination only exists at least in the early cases, and adequate drainage is most easily obtained.

In regard to the matter of whether sulfathiazole in an ointment base has any penetrating properties when applied locally, the work of Strakosch and Clark (23, 24) has demonstrated that a tissue concentration of 4 to 8 milligrams per cent may be obtained in the skin from the application of a sulfathiazole ointment comparable to what was used on our burn cases. Furthermore, in the extensive work of Ackman and Wilson, of Gurd, and their co-workers it was found that considerably higher tissue concentrations of sulfathiazole were obtained with their emulsion ointment when it was applied to raw surfaces which were not covered with skin. The results obtained by these two groups of workers establishes quite definitely that sulfathiazole can penetrate the tissues in sufficient concentrations to have a bacteriostatic effect when applied locally in an appropriate ointment vehicle.

Gurd and his co-workers have made several reports on the use of their sulfathiazole emulsion ointment in the treatment of burns. They have had very satisfactory results with this ointment in controlling infection in burned patients. The original report by Ackman and Wilson of the use of this emulsion ointment in the treatment of burns, as well as other conditions, appeared just prior to the article by Allen and associates (4), although the use of the sulfathiazole ointment was apparently inaugurated at about the same time. The extensive series of burns reported by Evans and Hoover which were treated by the application of a sulfanilamide ointment deserves mention as important additional evidence of the effectiveness of local sulfonamide therapy. With the use of their sulfanilamide ointment (6 per cent sulfanilamide in lanolin and cold cream) their problem of infections in burned patients has practically ceased to exist.

In reviewing the results of the burn cases in our series, it was rather gratifying to find that spontaneous healing occurred except in one case which developed an infection and subsequently required skin grafting. This series included a number of patients who were seen from 1 to 5 days after the burn and had positive cultures of Staphylococcus aureus hemolyticus and in some instances Streptococcus hemolyticus. The extent to which healing progressed under these rather unfavorable

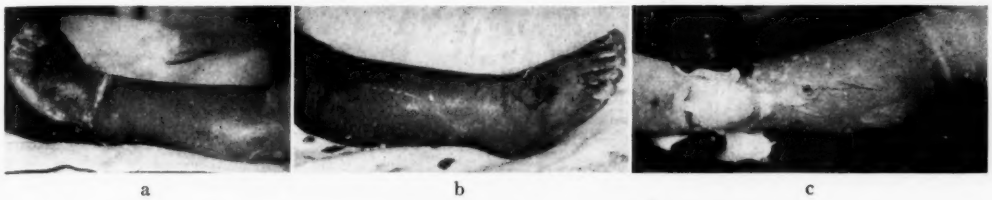


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Fig. 5. B. B., aged 21 months, received a hot water burn 5 days previously from bathtub accident. On admission the temperature was from 38.2 C. to 38.8 degrees C., the hematocrit was 36 per cent, and the plasma proteins were 4.6 grams per cent. a, Extensive burn of left foot and leg from just below knee at time of admission. Gentle cleansing, débridement, and irrigation with physiological saline solution was done and 5 per cent sulfathiazole emulsion ointment (petrolatum 48 per cent, arlacel C 2 per cent, water 45 per cent, tween 80 ¼ per cent) was applied on fine mesh gauze. Pressure dressing with mechanics waste was then put on. b, Extensive burn of right foot and leg from just below knee with dressing already applied to left leg. Cultures of both legs demonstrated heavy growth of Staphylococcus aureus hemolyticus. Both legs had appearance of second degree burn with probable areas of third degree burn. Blood transfusion of 160 cubic centimeters was given. c, Back of left leg at time of admission with detached layer of epidermis. d, Condition of burned legs 2 weeks after treatment with emulsion ointment, when original dressing was removed. There was little evidence of exudate on the dressing, the burned area was dry and healed. There were a few dry scaly crusts. Highest blood sulfathiazole level was 0.4 milligram per cent. e, Excellent condition of both legs 3 weeks after treatment, with complete healing.

circumstances appeared to us to be good evidence that the sulfathiazole had minimized infection sufficiently to permit the remaining epithelial remnants in the burned area to regenerate an epithelial surface. This spontaneous regeneration does not occur in the presence of a manifest infection or at least is very considerably retarded.

In view of our experience with a bacteriostatic agent in the local burn dressing, there would appear to be a place for some basic revision of the present classification of burns, to distinguish second degree burns which heal spontaneously from viable epithelial remnants in the burned area, from second degree burns in which these viable epithelial elements become destroyed or damaged by infection. For practical purposes this latter group are now classified as third degree burns because healing occurs only with the aid of skin grafts or after long periods of peripheral epithelization. It is this group of cases which offers a promising field for the use of local bacteriostatic agents to prevent infection and the destruction of epithelial remnants in the burned area from which spontaneous regeneration of an epithelial surface may occur.

The problem of the use of sulfathiazole or any other sulfonamide revolves to some extent about the matter of developing sensitivity to these drugs. In view of the widespread use of sulfonamides one may expect an appreciable incidence of sensitivity. There have been recent reports of a relatively high incidence of sensitivity to sulfathiazole ointment (10). With an ever-increasing number of people who have had some form of sulfonamide therapy, the time may come when the problem of sensitivity may contraindicate the use of a sulfonamide ointment on the burned patient unless a preliminary test has been carried out to eliminate the possibility of sensitivity.

a b c

Fig. 6. J. K., aged 2 years, received a hot water burn 2 days previously from bathtub accident. On admission the temperature was from 38.7 C. to 39.8 degrees C. on first day, hematocrit was 35 per cent, and the plasma proteins were 6 grams per cent. a, Extensive raw surface at time of admission over side of chest, axilla, and epigastrium. There were similar smaller areas on right side of chest and in right groin and on right side of buttock. Cultures from the raw surface demonstrated a heavy growth of Streptococcus hemolyticus and Staphylococcus aureus hemolyticus. Gentle cleansing and irrigation with physiological saline was done without general anesthesia. Five per cent sulfathiazole emulsion ointment (petrolatum, 48 per cent, arlacel C 2 per cent, tween 80 ¼ per cent, water 45 per cent) was applied on fine mesh gauze. Mechanics' waste pressure dressing applied. Blood transfusion of 200 cubic centimeters was given. b, Condition of burned area 2 weeks later when first dressing was changed. There has been considerable healing of the burned area of the chest as well as other regions. General condition of patient quite good at this time although for the first 5 days after admission there was moderate febrile reaction. The blood sulfathiazole level reached 1 milligram per cent. c, Almost complete healing of burned area on chest present at end of 3 weeks. The few remaining crusted areas were healed within another week. This case demonstrates that spontaneous healing may occur if a bacteriostatic agent is used in the local treatment.

However, for patients who are not sensitive to sulfathiazole, the use of sulfathiazole ointment for a burned area has given such gratifying results in our experience that this form of treatment for burns deserves consideration. Furthermore, in the extensive use of sulfathiazole emulsion ointment for burns and other wounds Gurd and co-workers have not had any serious difficulties from sensitivity, nor have Evans and Hoover from their sulfanilamide ointment.

A rather important point in the use of sulfathiazole ointment for burns is that no high blood levels were encountered in this series of cases. The maximum blood level was not more than 2 to 3 milligrams per cent even in cases with extensive raw surfaces. Gurd and his co-workers also found relatively low blood levels of not more than 3 to 4 milligrams per cent, when they used a sulfathiazole emulsion ointment in the treatment of burns or other wounds. This point is of considerable significance in the treatment of patients under conditions in which laboratory facilities are not adequate for determining sulfonamide blood levels. Evans and Hoover found blood levels of only 1 to 2 milligrams per cent when they used sulfanilamide ointment.

Furthermore, in severe burn cases in which urinary secretion may be considerably diminished, it would obviously be unwise to use sulfonamides locally unless the absorption rate could be controlled to some extent by a vehicle such as the ointment base described in this work which permits only a gradual liberation of sulfathiazole.

The systemic administration of sulfonamides in concentrations which are adequate to maintain a therapeutic blood level and an appreciable bacteriostatic effect in the burned area would also appear to have its disad-

vantages in the severely burned patients when kidney function as well as liver function may be diminished. If one can obtain a desirable bacteriostatic effect by the local application of a sulfathiazole ointment without the danger of overwhelming systemic absorption, it would seem unnecessary to subject a burned patient to the systemic administration of sulfonamides to obtain the desired local bacteriostatic effect, especially if there was appreciable impairment of renal and hepatic function.

With respect to the use of solvents, such as benzine, for removing heavy oil or grease from a burned surface, attention should be drawn to the fact that benzine is a powerful tissue irritant and is capable of producing a chemical burn in normal, intact skin. It is clearly undesirable to utilize such a solvent to remove grease from a thermal burn when in so doing, some degree of chemical burn is superimposed. Tests are being conducted to determine the most desirable surface active agent which might be utilized in an aqueous solution for removing grease to replace the need for using a solvent which has tissue-damaging properties. Our observations thus far would lead us to believe that tween 80, 5 per cent in physiological saline solution, will serve this purpose to a considerable extent.

In regard to the effect of the pressure dressings advocated by Allen and Koch and which were used in most of the burn cases reported here, it is probable that this has minimized to some appreciable extent the loss of plasma into the tissues or from the burned surface. It has not obviated, however, the need for plasma transfusions. In experimental and clinical observations on the rapidity of plasma loss after a burn, it would appear that a substantial part of the plasma loss may occur within the first half hour and unless the pressure dressing is applied within this length of time this original substantial loss would not be controlled. However, the control of subsequent loss would undoubtedly be favorably influenced by the pressure dressing. For the treatment of the plasma loss a chart has been devised by us (17) which is based on the hematocrit reading and the body weight. This has aided considerably in evaluating the plasma requirements of burn patients.

The pressure dressing undoubtedly influences the course of the burn patient from the standpoint of promoting the venous return from the dilated capillaries in the burned area. This point has not received the proper attention it deserves and, even if some choose to discount entirely the effect of the pressure dressing in minimizing plasma loss, there can be little doubt but what pressure is beneficial to the survival of skin which has been damaged by heat. In skin grafting it is frequently observed that venous stagnation may occur in the graft. If this is not controlled by pressure dressings a graft may slough off even after it has appeared to be a perfect take. This is especially true of skin grafts on the leg where the venous return is particularly poor when the leg is in a dependent position. If viable skin grafts can undergo necrosis from venous stagnation it is not at all improbable that burned skin which is on the borderline of viability may also undergo necrosis from venous stagnation which could otherwise be obviated by a pressure dressing. Aside from the favorable influence of the pressure dressing in aiding venous return the fundamental principle of utilizing the forces of gravity should not be overlooked in supplementing venous return by elevation of the burned part in so far as this is feasible.

For a complete discussion of the various aspects of burns reference should be made to the extensive work of Harkins.

SUMMARY

Sulfathiazole emulsion ointment (see formula page) was found to be very satisfactory in the treatment of burns and would appear to be especially suited to the first aid type of burn treatment when cleansing procedures may not be feasible because:

1. There is sufficient liberation of sulfathiazole from the ointment to have at least some bacteriostatic effect which is not obtained by grease dressings alone.

2. The liberation of sulfathiazole is controlled in this ointment preparation to the extent that overwhelming systemic absorption of the sulfathiazole does not occur. It is, therefore, feasible to treat burn patients with this ointment under conditions where it may

not be possible to follow the blood sulfonamide level by laboratory tests.

3. The liberation of sulfathiazole from the emulsion ointment is continued for a period of a week or more and thus permits a continuous bacteriostatic effect.

4. The sulfathiazole emulsion ointment has an analgesic effect on the burned surface which minimizes the extent of sedation required and thus keeps the patient in a relatively more ambulatory condition.

5. The emulsion ointment can be removed from burned areas with less difficulty than can ordinary grease dressings if it should be desirable to change the dressings.

6. The emulsion type ointment may be easily prepared from sterile ingredients when it is needed with a simple salad dressing mixer.

CONCLUSIONS

The principle of the use of a bacteriostatic medicament in a bland grease base containing surface active agents which aid in the liberation of the bacteriostatic medicament offers a promising approach to the problem of the local treatment of burns, especially from the standpoint of controlling infection.

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ROENTGENOGRAPHIC INTERPRETATION OF WHAT CONSTITUTES ADEQUATE REDUCTION OF FEMORAL NECK FRACTURES

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THE worth of any opinion cannot be evaluated until the facts and the interpretation of those facts on which the opinion is based are presented for consideration. The statements to follow are the result of observations made over a 6-year period. These observations include studies made of roentgenograms taken from large bone and joint services, of patients in private practice, and of cases of friends and associates. The series of cases used to illustrate this paper are taken from the writer's private practice.

No particular technique or gadget for the internal fixation of an intracapsular fracture of the femur is advocated. The fixation must be adequate, correctly placed, and in direct line of weight thrust. In this author's experience the cannulated Smith-Petersen nail has fulfilled the above functions better than have wires, screws, bolts, or multiple pins.

An excellent result in this type of fracture is one in which (a) there is no pain or spasm; (b) there is no limp; (c) there is equal leg length; (d) there is a complete range of active hip motion including full internal rotation; (e) the patient to walk and climb requires no external aid; (f) on roentgenographic examination, the neck is of practically normal length, the head is smooth with normal density, the joint space is maintained, and the fracture has healed with unbroken lines of trabeculation crossing the fracture site.

No attempt is made to evaluate the rôle of blood supply as a cause of nonunion or the development of a dead head. This paper deals with only the immediate results, that is, up to 5 years after internal fixation. The prognosis as to the ultimate fate of the femoral head of a fractured hip, in this writer's opinion, is guarded under even the most ideal conditions. This author believes that the immediate fate of the femoral head may be sealed at the time of fracture by receiving irreparable damage to its blood supply but that this accident is relatively uncommon. He believes, on the other hand, that the early fate of the femoral head is more often determined at the time of reduction. Further, he believes, that one can predict with a certain amount of accuracy from the roentgenographic views taken at the time the fixation is done which heads will unite and live and which heads will not unite and will die. All failures in the series of cases to be shown had one fault in common. All hips that healed did not contain this fault. Not only in this series, but in all the author's experience this has been the rule, not the exception.

Clinically, patients who are going to have good hips are well on their way toward this end by 5 weeks after fixation. Patients who are going to have poor hips at no time handle the leg well following fixation. Limp, groin pain, adductor spasm, lack of internal rotation, and lack of full active control the limb are present in all of these cases to variable degrees. From the time of fixation until the final check-up, these failures never do get along.

Three patients, not shown here, all women, were seen because of groin pain on weight bearing and motion. X-ray pictures taken with both hips in complete internal rotation showed slight decalcification about the affected hip with a suggestion of a break in the cortical continuity of the calcar femorale. No history of trauma could be obtained. Within 2 to 5 weeks all of these patients developed typical femoral neck fractures on the affected side. It is my belief that not a few typical femoral neck fractures are pathological in nature and that these people fall as a result of their hips breaking and not that the hip breaks as a result of a fall.

Before the study to be reported was begun, various methods of obtaining reduction and internal fixation were used. Open reduction was performed on hips previously reduced in the operating room and proved by roentgenograms and on hips not previously reduced. Closed reductions were done in the operating room with the patients in traction and on a fracture table. Closed reductions were also done with the aid of the fluoroscope, the fluoroscopic table and manual traction being used. Leadbetter's maneuver was carried out in many cases. The heel and palm test was tried along

From the Department of Bone and Joint Surgery, Northwestern University Medical School.

Presented before the Chicago Orthopaedic Society, December, 1943.

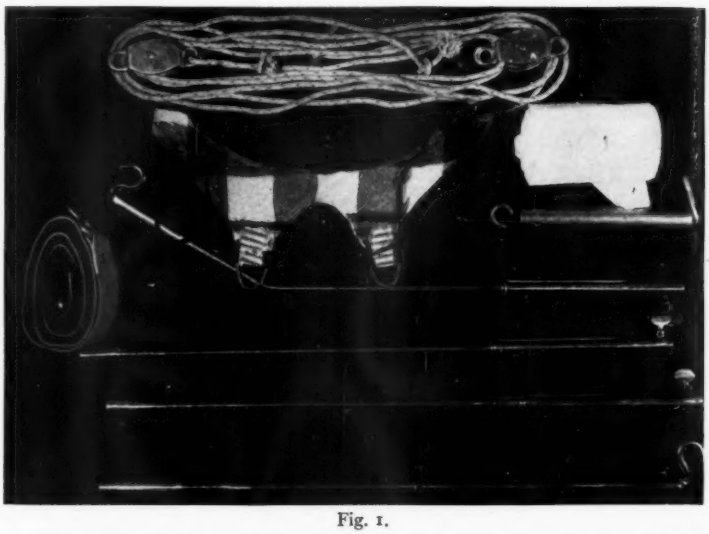

Fig. 1.

Fig. 2.

Fig. 1. Soutter apparatus dismantled showing traction bars, traction strap and felt, special hitch strap, double block set, sheet wadding, and spring balance. This apparatus offers traction to above 100 pounds and at the same time allows flexibility and movement of the part. It has been found invaluable for reducing old dislocations of the shoulder, dislocation of the hip, slipped femoral epiphyses, and many types of fractures. For reduction of intracapsular fractures, the patient is thoroughly anesthetized. The long traction bar is placed under the patient in the long axis of the body. The traction strap is placed in the groin and hooked to the head end of the bar. The sheet wadding is wrapped about the foot and ankle on the affected side and then the special hitch strap is attached over this. The spring balance is hooked to the hitch strap by the iron rings provided in the hitch strap. The balance is then hooked to the double block set which in turn attaches to the foot end of the bar. Traction is applied with the leg in *external* rotation and in about 10 degrees of abduction. From 60 to 80 pounds of traction, as read on the spring balance, is applied. The operator's hands are under the knee and with the traction on, gentle flexion of the hip to about 30 degrees is done a few times. Then the knee is grasped and if *complete* internal rotation can be achieved by very little force, reduction is probably satisfactory. When internal rotation occurs, the leg is then adducted by moving the Soutter bar toward the other leg. A small sand bag is placed under the knee to support it and prevent strain on the medial aspect which will result from the assistant's pressure. An anteroposterior roentgenogram is then obtained. If reduction is complete, an assistant holds the position obtained without any change until the whole fixation procedure is completed. No frogging or motion of any type is permitted.

Fig. 2. The special instruments required for this procedure. Hammer, assorted nails, sizes 4 to 4¾ inches in length, and cannulated to accept a 3/32-inch wire. Drill with Jacobs chuck. Nail, wire, and driver shown as a unit. Guide as developed by Edward Geckler of Philadelphia and modified with his permission, to accept the wire instead of screws. Starter—this is used to macerate the cortex of the femur before the nail is inserted. It is done by threading the starter over the wire, and then by gentle tapping until the starter enters the cortex, then disengaging the starter from the femur, turning it one-quarter turn, and repeating the procedure in this manner until the cortex has been softened. This will avoid splitting of the cortex and the turning of the nail edges. In using the guide the sharp pointed long rod is pushed through the skin until it hits the lateral aspect of the femur. It is then brought to the anterior surface of the femur, and then by lifting up on the handle the point keeps in contact with the femur constantly as it is worked up until the head is reached, then the point of the rod is firmly skewered into the head or acetabulum, as the case may be, to give firmness to the guide apparatus. The skin is incised, a transverse incision 1 inch long being made at the point indicated by the guide handle. The sharp-wire holder is thrust through the handle into the wound until it strikes bone, is fastened by the thumb screw, and the wire is drilled home. This wire must be new with an excellent sharp point, or difficulty will be experienced in starting the wire at such an acute angle with the shaft. The nail is then threaded over the wire, after the cortex is macerated, and is tapped home, not driven with force. Small fast strokes, of little power are all that is necessary or should be done to set the nail. While this is being done, the fluoroscope room is dark and the operator works by a red light handled by an assistant. Only the operator is surgically gowned.

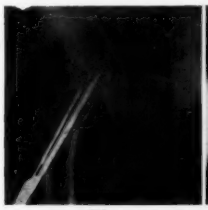

Fig. 3a.

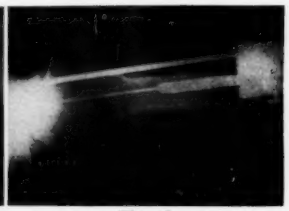

Fig. 3b.

Fig. 3. a, The guide is in place, the guide rod has been rotated slightly to show the guide wire entering the proximal fragment. Note that internal rotation is complete and no sign of the lesser trochanter is visible in the film. Unless this is true, *complete internal rotation* has not been obtained. The small white area on the inferior surface of neck marks the long cortical line of the femur, the *calcar femorale*, the true line of weight thrust. Note that the guide wire enters the femur *at or below the level of the lesser trochanter* and runs roughly parallel to the calcar femorale. The guide wire is now run into the head to the depth desired and anteroposterior and lateral films are taken. If the wire is at the right depth, another wire of equal length is thrust by hand through the wound close to, and parallel with, the guide wire. This second wire will strike the femur. The difference in length of the two wires at the operator's end is the actual length of the nail required. b, Lateral view, Figure 3, a, showing guide rod and guide wire in position. The guide wire should be the proper depth if direct measuring of the nail is to be taken as described. Following measuring of the nail, a good practice it is thought is to drill the wire deeper and into the acetabulum. This is an added factor in preventing any deviation of the head that might be caused by the nail as it enters the head.

with other devices. The conclusions after experiences with these methods were as follows.

Open reduction. The chief value gained here was the ability to compare the actual findings in the hip with the findings in the preoperative roentgeonograms. Thus developed a better roentgenographic interpretation of what constitutes a well reduced hip. The conclusions reached were (a) that any hip that can be well reduced without opening does not need an open procedure; (b) that the occasional hip in which reduction cannot be obtained while closed, should be opened; (c) that if good contact between the head and neck is gained with no anterior or posterior angulation of the head on the neck and the neck well under the head fragment, the fact that the head fragment may be rotated somewhat on the neck has no more effect on the healing than rotation following osteotomy for rotation deformity has on bone healing elsewhere in the body; (d) that if the hip is not reduced, previous to open operation, this writer knows of no more difficult piece of hip surgery, with the possible exception of correctly reducing and fixing a slipped upper femoral epiphysis, than is encountered in correctly reducing and internally fixing a femoral neck fracture by the open route.

Closed reduction. The fracture table was used. This table offers certain advantages but with the stiff unyielding traction of post and counter pull, the reductions were poor, great strain was on the knee, and all in all the plain wooden table with the cassette holder under its top, and traction pro-

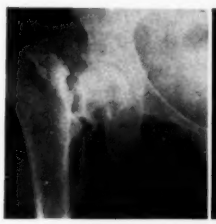

Fig. 4a.

Fig 4b.

Fig. 5.

Fig. 4. Shows nonunion of femoral neck fracture of 5 years' duration. This patient was operated upon by pulling shaft well down and then performing an intertrochanteric osteotomy. No attempt was made to freshen up the fracture site or to interfere with the capsule in any way. b, Same patient as Figure 4, a, 2 years after osteotomy. Patient walked without support 14 weeks following osteotomy. Four years after osteotomy condition of hip similar —patient leads active painless existence. Whether head is dead or not 4 years after operation, joint space is maintained, head is of normal shape, and previous union which was rapid, is present. Union occurred, as with fractures elsewhere, because weight thrust was direct, shearing and torsion forces avoided. Note internal rotation of shaft and amount of lesser trochanter that is visible. If the conditions existing here could be obtained in fresh femoral neck fractures, the possibility of prompt healing might be enhanced.

Fig. 5. Abduction type of intracapsular fracture. This type is impacted. These need not be fixed internally because most of them heal kindly. It is safer, however, to fix them—one feels more secure. Note almost complete internal rotation and degree of valgus of the head. Particularly note calcar femorale, and that the *neck fragment is under the head fragment.* If settling takes place, the neck, by itself, will support the head in correct line of weight thrust. This is similar to what is accomplished by intertrochanteric osteotomy. Some so called abduction type of fractures are not really this type at all. These readily fall to pieces. The same criteria used for determining adequately reduced adduction fractures can be applied in determining true or false abduction types.

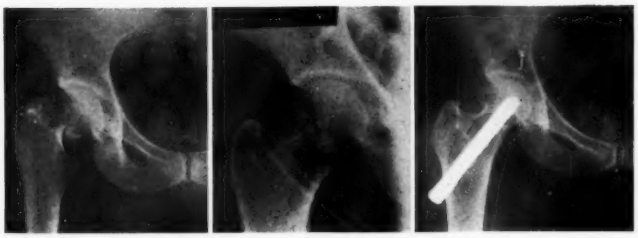

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Fig. 6. a, Adduction type of femoral neck fracture. Limb lies in complete external rotation with complete disengagement of fragments. All hips in this series are of this type. b, Same patient as in Figure 6, a. Spot film taken at time of reduction. Note complete internal rotation with absence of lesser trochanter. Note that neck fragment is *under and inside* of head fragment as judged by calcar femorale. This simulates the position obtained by osteotomy. The head is in valgus. If great traction is not applied with the leg in external rotation, it is difficult to get the neck by the head. Unless the neck gets beneath the head, complete internal rotation cannot be obtained because the neck fragment will hit the head, thus preventing reduction. Only anatomically or over-reduced fractures allow complete internal rotation. Once the above position is obtained *adduction* of the limb to neutral or slight adduction, throws the head into more valgus and gets the neck farther to the inside of the head. The neck, not the fixation material, takes the weight thrust from the head. c, Same patient as in Figure 6, b, 3 years after fixation. The neck fragment can still be seen under and inside the head supporting it. The shaft is thus prevented from using the head as a fulcrum and adducting and thus forcing the neck up and past the head to produce varus. In this case union has occurred. Internal rotation is free. Note direction of Smith-Petersen nail. It starts below the level of the lesser trochanter, runs parallel to the calcar femorale. The nail is preferred because in a correctly reduced hip, the nail acts only as a guide, which is in direct line of weight thrust, and its only function is to deliver the head in the proper position onto the waiting neck. The neck, itself, does the supporting; the weight thrust the impacting.

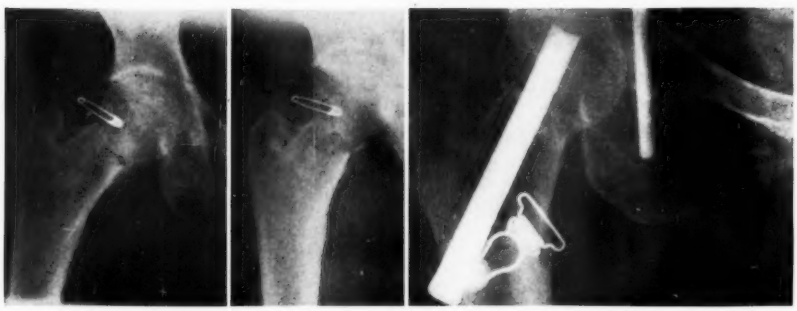

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Fig. 7. a, Spot film taken at time of reduction. Note that some abduction of shaft exists and that the neck is not truly under and inside of head fragment. This position is unsatisfactory. b, Same patient as in Figure 7, a, spot film taken after more traction, internal rotation, pushing medially over the trochanteric region, and *adduction* of shaft. Note change in valgus of head and that the shaft is now under and inside of head fragment. Position satisfactory. c, Same patient as in Figures 7, a, and 7, b, 15 months postoperative. Patient began weight bearing 5 months after fixation. Back at work full time without pain, limp, or support 9 months from fixation. Perfect clinical result to date.

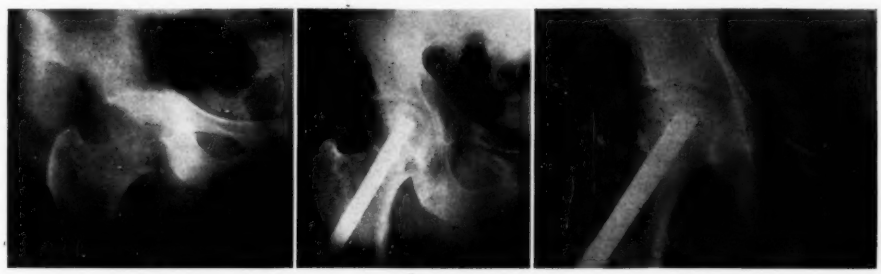

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Fig. 8. a, Spot film showing reduction. Note neck fragment *well under and well inside of head fragment.* The limb will now be adducted and fixation proceeded with. b, Same patient as in Figure 8, a, 2 months after fixation. This patient was allowed full weight bearing at this time through a misunderstanding. Note position of nail. Note that as the shaft attempts to adduct, instead of exerting tremendous force on the fixation material, the neck fragment tends to throw the head into more valgus by the leverage that is applied by the inner side of the neck to the head. The support is bone to bone. All the nail has to do is to act as a guide and also to prevent external rotation. Since this is accomplished, the head cannot get away from the neck. c, Same patient as in Figures 8, a, and b, 18 months since fixation. Note in region of calcar femorale, that the neck is well under and inside of the head fragment giving excellent support to the head in direct line of weight thrust.

vided by the Soutter apparatus was found the most satisfactory.

The safest method for the operator to adopt is blind nailing in the operating room without use of the fluoroscope. In this method the closer the dark room is to the operator, the less fatiguing to all.

Manual traction. This method failed to gain adequate reductions in many instances. The heel-palm test was found to be of little value in determining a reduction.

THE STUDY

There were 4 out and out failures in this group of 38 consecutive subcapital or transcervical fractures. Two of these failures are shown in the illustrations. The longest time from fixation in this series was 4 years and 8 months; the shortest time was 18 months. The youngest patient was 35 years of age. The oldest patient was 99 years of age. There was 1 death, the 99 year old patient died at the age of 102 years. All the other patients were living at the last check-up. There were 5 males in the series. There were no infections.

No impacted (abduction) fractures and no basilar fractures have been included in this series. All hips in this series were completely displaced and subcapital or transcervical in location. All patients have had roentgenograms of their hips every 3 months the first year and every 6 months thereafter.

Repeatedly it has been stressed by various writers that a good reduction of a femoral neck fracture should have the head in valgus with good contact between the head and neck. This paper will attempt to standardize the criteria of what constitutes a good reduction and then to show that these criteria are present or absent in the spot

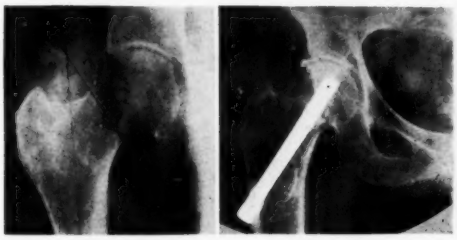

Fig. 9a. Fig. 9b.

Fig. 9. a, Spot film at time of reduction. Note the poor position of head, full internal rotation of shaft, but that *neck is under and inside of head fragment.* The head is in varus and if the neck was not under and inside of the head fragment, all weight thrust would be on the fixation material not bone against bone. If the shaft should then adduct the neck would readily slip by and upward in relation to the head. Compare with Figure 10, a. b, Same patient as in Figure 9, a, 2 years after fixation. No limp, no support, full motion, and no pain. Head has united in peculiar position but union has occurred. Note that the neck is well under and inside of head in region of calcar femorale supporting the head. All nails, with but two exceptions, have been left in place in all cases except the four failures. The 2 cases in which they were removed was because in 1 case the nail was too long, originally, and gave pain in the soft tissues. The other case is illustrated in this article, and the nail came partially out. In all other cases, except the failures, the fixation material did not shift.

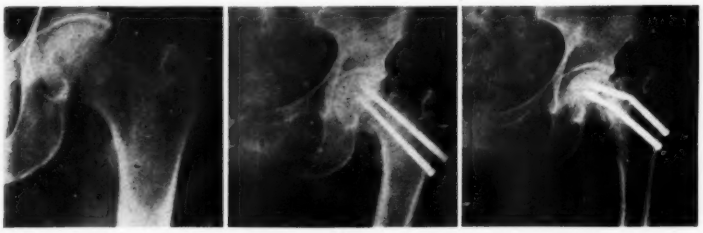

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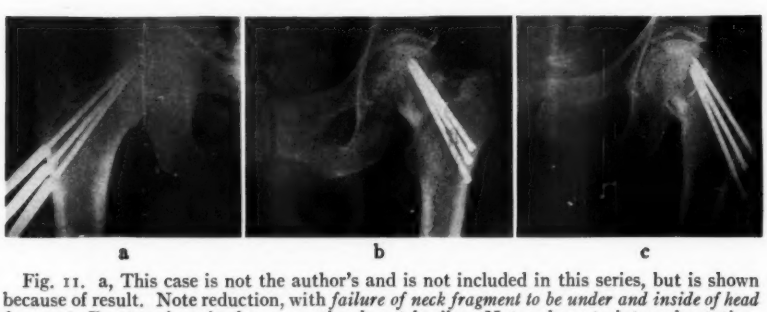
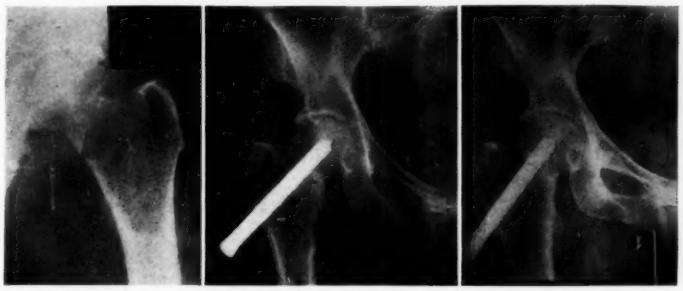
Fig. 10. a, Spot film at time of reduction. Note lack of internal rotation and in this case conditions are reversed and *the head fragment is below and inside the neck fragment.* In this instance adduction of the shaft on the head is allowed because the neck fragment does not support the head. Compare with Figures 8, a, and 9, a. b, Same patient as in Figure 10, a, 2 months after pinning. Note that shaft shows adduction which puts head into more varus. Nothing is supporting head except fixation material. Varus in these cases is produced by adduction of the shaft. If the *head fragment is below neck fragment,* adduction and angulation is permitted. If the reverse is true, the adduction is prevented by the neck fragment supporting the head and angulation cannot occur and weight thrust is delivered solidly against the head with no shearing or angulating forces able to act effectively. c, Same patient as in Figure 10, a, 9 months after fixation. This is not an end-result but it has gone to complete failure. Note density of head. Note how the head has been passed by the neck as adduction of the shaft occurred. The effect of this force is well illustrated in the fate of the screws. Any of the numerous fixation gadgets will probably hold a properly reduced fracture because no real strain is upon the fixation material. On the other hand, no material will hold in movable cancellous bone when shearing and torsion forces take effect. The material either breaks, migrates, or becomes loose because the force is not bone against bone, but metal against bone, an impossible mechanical and physiological set-up. It is, therefore, not very important what force is necessary to break or distract gadgets put in hips. If the gadget acts as a guide in line with weight thrust, allowing the head to settle on the neck with the force transmitted properly from head to neck, very little holding power is necessary, only rotation must be prevented.

The Smith-Petersen pin allows strength, rigidity, and being in one piece acts as an ideal guide. The nail itself has no effect on blood supply to the head, and in these cases the nail has not been removed except as noted and no ill effects have occurred. There are no main blood vessels in the center of these femoral necks and heads, except sclerotic ones near the fovea. Compare with Figure 11, a.



a b c

Fig. 11. a, This case is not the author's and is not included in this series, but is shown because of result. Note reduction, with *failure of neck fragment to be under and inside of head fragment.* Fracture is quite low on neck, almost basilar. Note adequate internal rotation. Note placement of fixation material. Note valgus position of head. Compare with Figures 7, a and b. b, Same patient as in Figure 11, a, 6 months after fixation and at time weight bearing was started. Typical of all failures—internal rotation was lacking, groin pain, adductor spasm, and limp with support were present, but mild. c, Same patient, 13 months after fixation. Note adduction of shaft, and how the neck has moved up farther in relation to head which is in varus. Nothing supports head fragment. Note density of head and productive reaction. This is classed as a failure. The movement of the unsupported head and shaft is what breaks the metal or sends it into the pelvis or works it out of the head. Compare with Figure 7, c.



a b c

Fig. 12. a, A spot film at time of reduction. Woman 56 years of age. Note marked obliquity of fracture line and lack of complete internal rotation. Fracture similar to that in Figure 13, a. The neck fragment, however, is *below* head fragment. In this way it differs from Figure 13, a. b, One year since fixation. Note external rotation of shaft and that the nail has been extruded. Note that shaft has adducted but that *neck stays under and inside of head fragment.* Patient at this time is walking without support, slight limp, no pain and is back at work teaching school. Occasional groin ache. Limb internally rotates to 5 degrees' external rotation and is one-half inch short. Patient has full control of limb. c, Two years since fixation—union present. Active motion full except internal rotation limited to neutral. Full normal activity. No pain except when lying on affected side when nail is bothersome. No support. Slight hesitancy in gait but no limp. One-eighth inch heel raise on affected side and one-eighth inch off heel on normal side balances for good gait. Estimated as a good but not an excellent result. Compare with Figures 4, b, and 13, d. Note increase in internal rotation between time of Figure 12, b.

films taken at the time of reduction. If the criteria at the time of reduction are satisfied, the results will tend toward the excellent. On the other hand, if these standards are lacking at the time of reduction, failure will result in many more instances than otherwise. In these failures nonunion, fibrous union, aseptic necrosis, extrusion of fixation material, shortening and deformity, will be commonplace. The changes in the head and neck that indicate impending failure of hip fixation were found to be present in the roentgenograms within the year from the time the fixation was done.

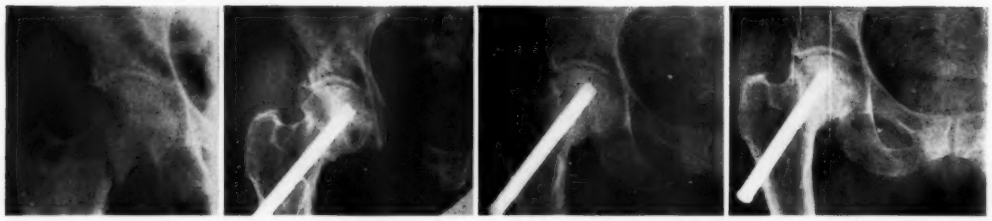
THE ROUTINE

At the time the fracture was first seen, Russell traction was applied. The patients were encouraged to move about, lift themselves up and down, to sit up, to roll and in all ways to keep moving. These fractures were not considered emergencies. It was felt, rather, that good medical care, the preoperative activity, and time to size the patients up, were important adjuncts in improving their chances.

All patients were turned from back to sides every 2 hours by the nurses. Involuntary pads were placed under them and all effort was made to keep these people clean and dry. If rubber sheeting was between the mattress and sheets, it was insisted upon that a mattress protector be placed on top of the rubber sheet and then the bed sheets over this. By this method pressure sores were not encountered. If it was not insisted upon that each patient turn herself or was turned every 2 hours, the floor care was desultory and the patient became wet, developed excoriations, and bed sores. The nurses would only notice trouble and remedy it if the patient was turned. If the patient was not turned, good back hygiene was usually lacking.

In about 10 days if the patient was active and comfortable, the operation was proceeded with. In this series the routine premedication was 1/12th grain morphine and 1/150th grain atropine. No morphine after surgery was allowed. Pentothal sodium was used in all cases for induction and relaxation. After reduction the pentothal was either discontinued or a slow drip was started and the patient was carried on a mixture of 60 per cent nitrous oxide and 40 per cent oxygen. This combination was the most satisfactory type of anesthesia we have tried. It is, in our hands, far superior to spinal or local anesthesia. Spinal anesthesia produced various types of reaction and local anesthesia failed to give enough relaxation.

All reductions and fixations in this series were done on the fluoroscopic table. The fluoroscope had a spot film attachment, but this is not an absolute essential. The portable x-ray unit was used to obtain the lateral views.

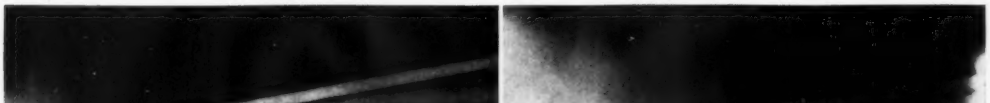


a b c d

Fig. 13. a, Spot film at time of reduction. Patient is a woman 58 years of age. Note obliquity of fracture line and complete internal rotation. The *neck fragment*, however, *fails to be below and inside of the head fragment*. There is no bony support to prevent shearing thrusts. Compare with Figure 12, a. b, Hip 6 months after fixation. Note complete internal rotation, direction of nail, and that *head fragment can be seen extending below and inside of the neck fragment*. The fracture site, otherwise, appears to be uniting. Weight bearing started at this time. Compare with Figures 6, b, and 11, a. c, One year since fixation. Note complete internal rotation. Nail remains in position. Note adduction of shaft and relation of shaft to head. Productive reaction about fracture site. Fibrous union with nothing to prevent shearing forces working against the unsupported head. All support is being taken by the nail and not by the femoral neck. Patient at this time is walking with marked limp, uses cane, and has pain in groin with adductor spasm and some flexion deformity. Unable to do housework without pain but is active. Full active control of limb is absent. d, Two years since fixation. Note changes in and about femoral head. Internal rotation still present. Nail remains in position. Note adduction of shaft. Patient uses cane, lacks full active control of limb, has pain and marked limp, but does housework with difficulty. This is a failure. Are the vascular and productive changes seen in this and other failures due to the original trauma or are they the result of a poor mechanical set-up, resulting in chronic irritation and altered physiology which nature reacts to by attempting to wall the offending part off and sequestrate it?

The fluoroscope was used to introduce the guide. This step took but a few seconds and once the guide was correctly placed, all checking by the operator was done from roentgenograms.

The roentgenologist or a technician trained in this work handled the fluoroscope and the taking of the x-ray films. This arrangement eliminated wasted time, minimized the exposure of the operator, and enabled him to work efficiently without contamination or bother. The judging of the depth of the guide wire and the depth of the nail, along with the taking of the films, all were supervised by the person operating the fluoroscope. The operator checked these observations in the roentgenograms. The time to complete the whole procedure from reduction to wound closure was from 60 to 80 minutes. About 20 minutes of this time was consumed by the actual operation.



a b

Fig. 14. a, Spot film, lateral view, of reduced fracture. This view shows a backward tilting of head because not enough internal rotation has been produced in spite of the disappearance of the major portion of the lesser trochanter in the anteroposterior view. The guide wire enters the head in the anterior portion, but centers the neck. By gentle manipulation, all internal rotation possible has been gained. To correct this position, the Smith-Petersen nail is threaded over the guide wire and is gently driven into the neck to a depth approaching the fracture line. The guide wire is then drilled out of the head until its point is hidden by the nail. The nail driver is then reattached by threading it over the wire and screwing it into the nail. Using the driver handle as a lever, internal rotation is easily increased to the desired amount. The knee is held in the new position by the assistant, the guide wire is driven into the head again and anteroposterior and lateral views are obtained. If satisfactory, the nail is driven home. X-ray films again check the final result. b, Same case after procedure described in 14, a, has been completed.

No hip can be considered internally fixed until perfect anteroposterior and lateral views have been taken proving without doubt that the fixation material is well centered, of proper depth, that no twisting or angulation of the head has occurred, and that proper reduction is maintained in both planes. So important is this one point that no hip should be internally fixed where an excellent, clear lateral view cannot be obtained.

All figures in this article and all patients in this series had excellent lateral views showing the fixation material engaging the head in a satisfactory manner. It was not enough to have the views showing the guide wire in correct position, but these views were repeated after the nail had been driven home. While the nail was being tapped home, the roentgenologist viewed its progress at times while the operator stepped away. This was done so as to avoid the nail catching the wire and driving it ahead toward the pelvis. If the wire did move, it was drilled farther in or out as the case required so as to prevent the tip of the nail from engaging the bent portion of the wire.

To date, this writer has never had a shaft or head split or fracture from the introduction of fixation material.

Following operation the patients were again placed in traction. The patients were required to sit up, roll, and to be turned every 2 hours. They were encouraged to lift themselves about in bed with the aid of the cross bar dropped from the Balkan frame.

No attempt was made to hurry these people out of bed. If, as in all of this series, they did well in bed, they were kept down from 3 weeks to 12 weeks, depending upon their age, size, and ability to handle themselves. Exercises, such as deep breathing, leg and arm movements, were given. Daily physical therapy to the knees and feet in the form of massage and exercises was started about the fourth day after fixation. Weight bearing was started from 4 to 6 months after fixation. No braces or calipers were used.

From both the mortality and morbidity standpoints, this author has had far more trouble in people with fractures about the trochanters than he has experienced with the group presented here.

The illustrations are used to emphasize the principal points brought out in this article.

SUMMARY

The suggestions for standardization of what constitutes adequate reduction of intracapsular femoral neck fractures are presented.

These suggestions are the result of studying numerous roentgenograms over a 6 year period and of attempting to find certain characteristics which were present in those roentgenograms in cases that were successful but which do not obtain in roentgenograms of cases that were not successful.

The method described for obtaining reduction of femoral neck fractures is based on complete relaxation under an anesthetic and then pulling the limb down in external rotation and slight abduction. While the traction is on, gentle flexion and toggling of the hip is carried out until the neck passes the head. The limb is then internally rotated to its limit. No resistance should be felt in carrying out this maneuver. The patella should face directly medially and the internal femoral condyle should be directly on the small sandbag that supports the knee. When this position is obtained, the limb is adducted to neutral or slightly beyond. An anteroposterior and, if desired, a lateral film is now taken.

If in the anteroposterior view, the criteria are satisfied, the guide is inserted, the guide wire is put in, and anteroposterior and lateral views are now taken. If the wire is perfectly centered in both views and the hip is reduced in both views, the nail is driven home. Anteroposterior and lateral x-ray films check the depth and position of the nail and the reduction. If these are satisfactory, the guide and guide wire are withdrawn and the wound is closed.

The technique described here for fixing hips internally is not advocated but is described to illustrate certain points.

The reduction is applicable to the operating room, and a flat wooden table with a cassette box under its top proves as satisfactory as any table. The Soutter apparatus has been the most satisfactory method of applying traction.

All standards described in this paper are based on roentgenograms taken with the limb in full internal rotation. In this way the neck length is established. If the roentgenograms in this paper are studied, one will note that the head and neck are separate from one another and there are no overlapping shadows where a portion of the neck covers a portion of the head. If overlap is present, it means that a complete reduction has not been obtained because if complete internal rotation is present any overlap indicates overriding or angulation, but not end-to-end contact. Any x-ray view short of complete internal rotation distorts the relationship of the head and neck and makes interpretation of the film practically worthless.

A satisfactory reduction is one in which the limb is in complete internal rotation and at least neutral lateral position. The neck fragment is *well under and well inside* the head fragment as

shown in the anteroposterior view. In the lateral view the head and neck are in line with no angulation and no overlap. The fracture surfaces are apposing one another.

A satisfactory fixation is one in which the fixation material enters the shaft of the femur *at or below the level of the lesser trochanter*, runs through the lower one-half of the neck parallel to the calcar femorale, and centers the head in both planes.

The main purpose of the fixation is to act as a guide which allows the head to settle on the neck in a position in which the weight thrust is directly applied to the fracture site without shearing or torsion forces being exerted on the fixation material. The position that the femoral head and neck should assume to gain this objective has been described.

CONCLUSION

This author does not wish to insinuate that there are no failures in a comparatively large number of hips that have been internally fixed since the series reported here was closed. He has had failures, but the point he wishes to stress is that all the failures have occurred in hips that have been imperfectly reduced. That is, the neck fragment has not been placed well under and well inside the head fragment.

These failures have been due to many factors such as inability to obtain correct traction, inability to obtain adequate lateral roentgenograms, poor anesthesia, personal carelessness, and occasionally inability to obtain satisfactory reduction of the hip under ideal conditions.

In closing, an appeal is made first, for the fixation of hips in a place where all factors are in the patient's and the operator's favor; second, that if a hip cannot be reduced or if there is doubt as to the effectiveness of reduction, either an immediate intertrochanteric or a subtrochanteric osteotomy be performed as the case may require; and, third, that if a hip is fixed, but is not doing well, at the first signs of failure an osteotomy be done.

If a plan similar to the above is carried out it should aid in reducing the amount of disability now following intracapsular fractures of the femoral neck.

SUPPORTIVE IMMOBILIZATION OF THE CERVICAL SPINE

EDWIN BOLDREY, M.D., San Francisco, California

SUPPORTIVE immobilization of the cervical spine following a period of skeletal traction or when such traction is undesirable or contraindicated has been an annoying neurosurgical and orthopedic problem, the attempted solution of which has brought forth numerous devices of varying merit. The usual cast or splint is built up beneath or around the chin to such a degree that eating is greatly interfered with; if the jaw is permitted movement, there is likewise movement in the cervical spine. The result has been a failure to support or to immobilize or both. Cone[1] circumvented this difficulty by a plaster-of-Paris cast which encircled the forehead and from which reinforced prongs extended forward beneath the ears to lie along the maxillary arch below the zygoma. The cast then extended over the neck posteriorly and laterally and was continuous with a body jacket. The mandible and throat were entirely free. Sometimes the maxillary prongs were connected over the bridge of the nose.

The disadvantage of this apparatus lay in its size and weight and in the difficulty in maintaining satisfactory apposition of patient and plaster during the process of setting. A further disadvantage shared by all methods employing plaster of Paris as the means of immobilization after skeletal traction for fracture, dislocation, or fusion of the cervical spine is the tendency for syncope to appear when the patient sits up as is usually deemed necessary if a properly fitting cast is to be applied.

It appeared that the unsatisfactory aspects of the Cone type of cast might be avoided by a properly fashioned brace, and the following plan was drawn up. It calls for an aluminum cup molded to the occipital and suboccipital region and projecting laterally, partially encircling the ear. This cup is attached by steel bars to padded spinal, shoulder, and trunk bars. From the supra-auricular part of the cup a broad webbed strap connected by buckles to similar webbing padded with felt holds the head firmly in the cup and helps to

From the Division of Surgery, University of California Medical School, San Francisco, California.

[1]Dr. W. V. Cone developed this cast several years ago at the Montreal Neurological Institute.

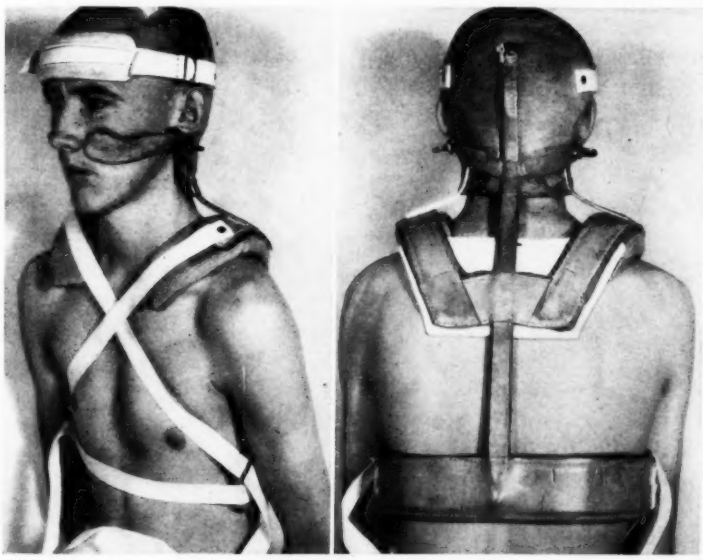


Fig. 1. Front and rear views of apparatus.

eliminate flexion-extension movement. From the infra-auricular part of the cup and connected by a ball and socket (universal) joint, a prong, made of aluminum molded to the contour of the maxillary and infrazygomatic region is carried to the vicinity of the nasolabial fold. This prevents rotation and further impedes flexion or extension of the neck. The whole is covered with soft leather. Shoulder and trunk braces are stabilized by buckled webbing.

This proposal was outlined to Mr. Gus Kern, brace maker for Children's Hospital in San Francisco, who then constructed the splint shown in the illustration (Fig. 1). The patient for whom it was tailored was a boy of 17 convalescing after a fracture involving the atlas and axis which had been treated by skeletal traction with Crutchfield tongs. Fittings of various parts of the splint were carried out with the patient still in traction and in bed. The splint was applied while he was recumbent so that he had immobilizing support when he first was brought into the erect posture.

The effectiveness of any device to prevent movement is determined to a large degree by the care employed by the brace maker in fitting it to the individual. In this case there was no observed movement of the patient's cervical spine, either when chewing movement or when voluntary cervical motion was attempted. The patient reported the splint to be comfortable; he wore it continuously, night and day, for a period of 6 months without objective or subjective evidence of difficulty.

Though occasion has not yet arisen, it is believed that the brace could be sufficiently standardized to serve as a splint for emergency transport after injury to this region. Its advantages over Wagoner's[2] splint are its design, primarily for cervical fracture, and the infrazygomatic splints which provide additional stabilization. For satisfactory convalescent supportive immobilization, however, an individually tailored brace will continue to be necessary.

Wagoner, George. U. S. Naval M. Bull., 1942, 40: 190-191.

EDITORIAL

SURGERY
Gynecology and Obstetrics

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JANUARY, 1945

THE RÔLE OF THE SPECIALIST IN MILITARY MEDICINE[1]

THE rôle of the specialist in military medicine has always been a vexing problem. Quite naturally the tendency among military men is to feel that all military physicians must be ready to meet any and every medical or surgical emergency which might arise on isolated posts, and that consequently every military physician must be a general practitioner with a high degree of specialized skills. There can be no doubt that the level of all around specialized medical knowledge which has been achieved in the medical services of our Army and Navy is of a high order, higher indeed than is true for the average general practitioner of civilian life.

This is a great achievement; yet, it would be shortsighted to allow an analysis of the problem to stop at this point. One still must ask whether in addition to this body of highly trained "general practitioners" of military medicine, the armed forces do not need the practical skills and the scientific leadership of the highly trained specialist. If so, organizational plans must solve the following problems: (1) how to attract specialists into the armed services, (2) how to give those military physicians who want to become specialists an opportunity to develop in this direction, (3) how to hold such men when trained in the armed services, and (4) how to plan the relationship between the specialist and the general practitioner in the armed services.

The pros and cons of these problems have recently been presented in an article entitled: "The Problem of Specialization in the Medical Services of the Regular Army and Navy Prior to the Present Emergency."[2] This article presents statistical data which indicate that prior to the present emergency the representation of the medical departments of our armed services was very low in national medical and scientific societies, and among the diplomates of our specialty boards.

It seems apparent that the existing tendency to try to make of *every* military physician a general practitioner, while understandable, has two drawbacks so serious as to overshadow any advantages. In the first place it makes it difficult to induce and attract men of top flight ability to make a life career of military medicine. (If anyone doubts this, let him consult the records of our best medical schools for the last twenty years, and see how many of those who graduated in the upper quarter of the class entered the regular Army or Navy medical departments.) In the second place, it results in confusion, loss of time, and loss of efficiency, whenever an emergency arises.

[1]This editorial was written by Dr. Kubie at the request of the Editors.

[2]Bull. New York Acad. Med., 1944, 20: Sept.

In this war, as in World War I, there was an initial period of fumbling and uncertainty which lasted for about two years, before the civilian specialist was used according to his specialized skill and training. At first there was an abortive effort to make of every specialist a general practitioner. Gradually this petered out, and the offices of the Surgeons General of the Army and Navy were reorganized into a pattern that approximates more closely that of a well run medical school or general hospital, with divisions representing each relevant specialty, usually under the leadership of civilian specialists. Because of the late date of such reorganizations, however, it has never been possible to alter the Tables of Organization of medical installations completely enough to give the specialties effective representation through the lower echelons. The start in this direction is only under way as the end of the emergency approaches. Furthermore, immediately after the last war, the pendulum swung back; most of the specialty divisions were dissolved, and the Surgeon General's Office returned to the prewar nonspecialized organizational plan and policy.

It is our contention that this should not occur again. Our national societies and our national specialty boards thus seem to have a manifold duty. (1) They should maintain close permanent liaison with the offices of the Surgeons General of the Army and of the Navy. (2) They should encourage among their own membership the organization of Army and Navy specialist reserve corps, as active units with periodic tours of training with military units, and periodic refresher courses. (3) They should urge and support plans for a permanent organization of the Surgeon General's offices along lines which will permit representation of all relevant specialties, with correlated changes in Tables of Organization from the highest echelon down as far as is necessary into the lower units. (4) Above all, our national specialty societies and our national specialty boards should use their prestige and authority to make sure that young medical officers, who have the aptitude and the desire to become specialists, should have the opportunity to make careers as specialists within the armed services, with opportunities for specialized clinical experience and for research and teaching in their special fields.

Our position cannot be better summarized than in the words of the late Thomas Salmon as quoted in the article already referred to: "I imagine that there will be no dissent from the statement that the regular establishment needs to have the important specialties adequately represented at all times in its own personnel. If there were no other reason, the retention of young medical men who enjoy military life, but who would leave the service if not permitted to work along the lines of their special interests, would be sufficient, in the present shortage of medical officers. Unless special, as well as general, tasks in military medicine are systematically undertaken in peace, it will be useless to expect regular officers, who will occupy high administrative positions in war, to know how to use specialists to the best advantage. Hostility or at least skepticism will be their attitude if they are thrown into contact with those working in special fields with no previous association as a basis for mutual understanding and respect. It is equally important that specialists should know how to work in the Army. Many a highly trained specialist from civilian life was less able to apply his skill to the actual problems of military medicine because he insisted upon conditions that could not possibly exist in a military organization."

This was the wise advice of a specialist, who never in his civilian career had been narrowly specialized, who had exceptionally wide experience in co-ordinating the work of general practitioners and specialists in the problems of civilian medicine, and who saw service in our army throughout the years of the last war as chief of the psychiatric division.

LAWRENCE S. KUBIE

THE SURGEON'S LIBRARY

REVIEWS OF NEW BOOKS

THE comprehensive treatise by Adams entitled *Intravenous Anesthesia*[1] consists of a review of all the available literature on intravenous anesthesia from its inception until the present time, and of all the drugs that have been administered intravenously to produce anesthesia, the various methods employed, and the results obtained. The volume is so arranged that it can be used readily for reference work. The chemical and pharmacologic aspects of the drugs are discussed in detail and separately from the clinical aspects. The discussion of the clinical effects includes a consideration of the use of the drugs in special fields.

Each chapter and the discussion of each agent are subdivided into four main sections: history, chemistry, pharmacology, and clinical use. The sections regarding clinical aspects are further subdivided into discussions on the use of the various drugs for surgery, medicine, obstetrics, psychiatry, and so forth. Each chapter has its own set of references with an extensive bibliography, thus making the book suitable for reference work.

Attempt has been made to have the nomenclature conform with the chemical and pharmacopeial terminology, as approved by the Council on Pharmacy and Chemistry of the American Medical Association —a task particularly difficult because of the great confusion now present in terminology.

The foreword is written by John S. Lundy, and constant reference is made to him, whose preliminary work, intimate knowledge, and enthusiasm for this subject have helped elevate intravenous anesthesia to its present position. The chapter on the historic considerations is detailed and complete.

The various agents which can be administered intravenously to produce anesthesia have been classified in tabular form, and include volatile and nonvolatile agents, local anesthetic agents, the urea derivatives, the inorganic salts, narcotics, hypnotics, and barbiturates. Each agent is discussed separately in detail in the following chapters, the advantages enumerated and the experimental clinical work with them recorded. The author's wide experience and excellent manner of presentation make his description of the technique of intravenous injection interesting. A set of illustrations show the various techniques of administering pentothal and the apparatus now available.

The chapter on evipal sodium carries the most extensive bibliography, including 482 references and 236 relevant articles not referred to in the text.

The chapter on pentothal, however, presents most of the author's own investigation and data and it is the most detailed and complete. Pentothal sodium at the present time offers the optimum as a close to ideal intravenous anesthesia. The chemistry involved in the manufacture of the agent, its effects on the various systems of the body, the pathological changes involved, and its clinical application are discussed in detail, as are the preparation of the patient, preliminary preparation of the drug, and the technique of administration. A table of the signs of anesthesia produced by 2½ per cent solution of pentothal sodium is interesting and can be used to great advantage for teaching purposes. A detailed discussion is presented of the untoward effects and also of complications, indications and contraindications, and military applications. The bibliography is extensive and complete.

A chapter is devoted to the analeptics and another very excellent chapter to the military surgical application of the intravenous anesthesia.

Intravenous Anesthesia is an extensive detailed report on all of the data available pertaining to the subject. It is a reference book which can be well utilized by the student of anesthesiology as well as the investigator interested in research. The compilation of the volume must have involved years of work and study. Its publication is welcomed by the specialists in anesthesiology; it brings up-to-date a subject whose life's span is only a few decades and whose future must certainly be considered as an integral part of the future of anesthesia. MARY KARP.

PLANNED timing in the treatment of wounds, particularly burns, is the motif of the book *Technique in Trauma*[1] by Fraser B. Gurd and F. Douglas Ackman. The book is very short and consists of three sections covering 60 pages and has numerous illustrations.

In the first section the authors review the problem of the treatment of burns and explain their conception of the principles upon which successful management should be based. They emphasize timing in treatment to anticipate the dangers and difficulties arising during the different periods associated with severe burns, namely shock, toxemia, sepsis, and repair. The general measures employed to anticipate and prevent shock, toxemia and infection are principally those which have been emphasized in other recent articles. The local measures advocated for the

[1]INTRAVENOUS ANESTHESIA. By R. Charles Adams, M.D., C.M., M.S.(Anes.). New York and London: Paul B. Hoeber, Inc., 1944.

[1]TECHNIQUE IN TRAUMA; PLANNED TIMING IN THE TREATMENT OF WOUNDS INCLUDING BURNS. By Fraser B. Gurd, M.D., C.M., and F. Douglas Ackman, M.D., C.M. Philadelphia, Montreal, and London: J. B. Lippincott Co., 1944.

prevention of infection and the promotion of rapid healing without formation of contractures, include gentle cleansing of the wound with soap and water, the removal of débris and devitalized tissue, the employment of pressure dressings incorporating curtain drainage and a 5 per cent oil-in-water emulsion of sulfathiazole, and the early grafting of skin.

In the second section over 200 major and minor burns were reviewed and from this group 100 major cases requiring hospitalization were selected for analysis. Eight-six of the cases had 30 per cent or less involvement of the body surface and 14 had more than 30 per cent. With the method of treatment advocated, 6 of a total of 7 deaths occurred in the 14 extensive burns.

Short discussions of various subjects are included such as the assessment of the damage produced by the burn, the value of sulfonamide treatment, reconstructive grafting, and the treatment of anemia and hypoproteinemia.

In section 3, a similar plan of timing in the treatment of wounds other than burns is presented. This treatment consists of the application of efficient first-aid, débridement, surgical antisepsis, occlusive dressings changed infrequently, and rest.

Although the authors used no controls in determining the prophylactic value of local sulfonamide therapy, they have a profound impression that the addition of 5 per cent sulfathiazole in an oil-in-water emulsion gives an important additional safety factor against invasive infection and provides a medium for adequate curtain drainage. No invasive infections were noticed, and the control of pre-existing infection was prompt and satisfactory. On the other hand they do not believe that sulfadiazine administered generally is indicated in severely burned patients except for unusual complications. In the opinion of the writers it may produce a grave and unnecessary risk to the liver and kidneys at a time when toxic manifestations from the burn itself are imminent.

Throughout the book the authors emphasize the importance of adherence to basic physiological and surgical principles and the application of these principles by the use of planned timing and teamwork. Clear-cut and controlled evidence is needed, however, to demonstrate the value of sulfonamides administered either locally or systemically in reducing the incidence and severity of infection developing locally in burns or other wounds.

W. A. ALTEMEIER.

IT is impossible in a few paragraphs to present an adequate review of Dr. Bunnell's excellent treatise on the surgery of the hand.[1] His book represents the work of a surgeon's lifetime—of painstaking and persistent application through many busy years to the problem of refashioning and restoring injured hands. This task involves many of the fundamental problems of surgery—the healing and repair of soft tissues, of tendons, of nerves, and of bone; the transplantation of skin and subcutaneous tissue, of tendons and nerves; the prevention and control of infection; the treatment of tumors, both benign and malignant—to mention only the outstanding ones. The problem as a whole involves a complicated and important mechanism whose function depends primarily upon the integrity of its parts and upon their freedom of movement. To secure restoration of function in such a mechanism after extensive destruction of tissue has occurred and after partial or complete fixation of structures that should move more fully has taken place requires infinite patience, imagination, skillful technique, and plain hard work.

No one can doubt in studying Dr. Bunnell's book that he has brought all these in full measure to the performance of his task. He has told and depicted with skill and imagination the problems he has faced, the treatment he has evolved, and the results he has obtained. Every surgeon who is interested in the surgery of the hand has been awaiting the opportunity of consulting and studying a comprehensive treatise such as Dr. Bunnel has prepared. We are indebted to him and grateful for this splendid contribution.

SUMNER L. KOCH

[1] SURGERY OF THE HAND. By Sterling Bunnell, M.D. Philadelphia, London, and Montreal: J. B. Lippincott Co., 1944.

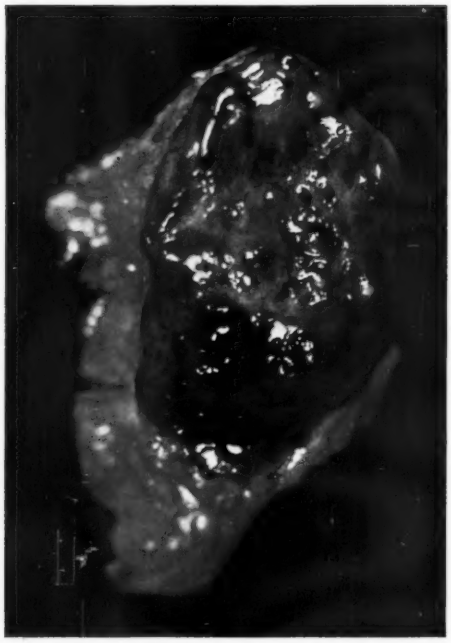

Fig. 1. Endometrioma of bladder wall showing typical gross appearance of a "chocolate cyst."

Endometriosis of the Bladder and Ureter.
—Vincent J. O'Conor and J. P. Greenhill.